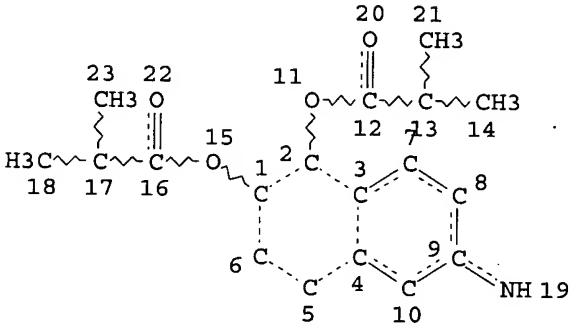
SN 10/030114

to oversome 07/16/03

ENTER (DIS), GRA, NOD, BON OR ?:bon 9-19 s, dis



ENTER (DIS), GRA, NOD, BON OR ?:end
L1 STRUCTURE CREATED

=> save temp l1
ENTER NAME OR (END):sn10030114/q
QUERY L1 HAS BEEN SAVED AS 'SN10030114/Q'

=> search l1 sss full
FULL SEARCH INITIATED 11:39:10 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 58862 TO ITERATE

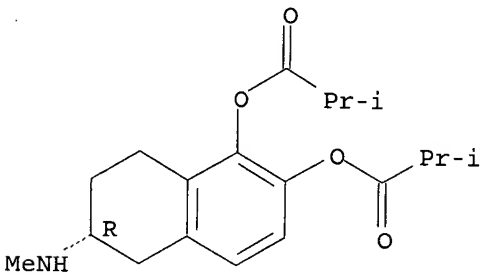
100.0% PROCESSED 58862 ITERATIONS 30 ANSWERS
SEARCH TIME: 00.00.01

L2 30 SEA SSS FUL L1

=> dis l2 1- sub bib abs
YOU HAVE REQUESTED DATA FROM 30 ANSWERS - CONTINUE? Y/(N):y

L2 ANSWER 1 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 373380-13-3 REGISTRY
CN Propanoic acid, 2-methyl-, (6R)-5,6,7,8-tetrahydro-6-(methylamino)-1,2-naphthalenediyl ester, hydrochloride (9CI) (CA INDEX NAME)
OTHER NAMES:
CN (+)-(R)-5,6-Diisobutyroyloxy-2-methylaminotetralin hydrochloride
FS STEREOSEARCH
MF C19 H27 N O4 . Cl H
SR CA
LC STN Files: CA, CAPLUS
CRN (146085-52-1)

Absolute stereochemistry. Rotation (+).



HCl

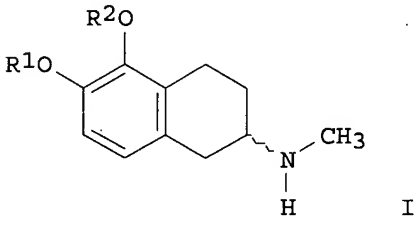
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1

AN 135:357780 CA
TI Optically active 2-aminotetralin derivatives, the processes for the preparation thereof, and the therapeutic use of pharmaceutical compositions containing them as antihypertensives, etc.
IN Amari, Gabriele; Del Canale, Maurizio; Razzetti, Roberta; Monici Preti, Pier Alessandro; Rondelli, Ivano
PA Chiesi Farmaceutici S.p.A., Italy
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001085668	A1	20011115	WO 2001-EP5212	20010508
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	IT 2000MI1053	A1	20011112	IT 2000-MI1053	20000512
	EP 1280759	A1	20030205	EP 2001-940415	20010508
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	NO 2002005393	A	20030113	NO 2002-5393	20021111
PRAI	IT 2000-MI1053	20000512			
	WO 2001-EP5212	20010508			

GI



I

AB The invention concerns the use of the optically active forms of 5,6-dihydroxy-2-methylaminotetralin and their acyl esters, namely I [R1, R2 = H, C1-4 acyl], and their pharmaceutically acceptable salts, as medicaments. Also disclosed are a process for prepn. of I, and the use of I in pharmaceutical compns. Examples illustrate the prepn. of (+)- and (-)-I [R1 = R2 = isobutyroyl (II)] and the biol. activity of (+)- and (-)-I [R1 = R2 = H (III)]. For instance, (.+-.)-II.HCl was resolved using (-)-L- and (+)-D-dibenzoyltartaric acids to give (+)-(R)- and (-)-(S)-II.HCl with > 99% enantiomeric excess (ee) in both cases. Alternatively, 3-methoxycarbonylamino-5-(2,3-dimethoxyphenyl)-2,5-dihydrofuran-2-one underwent asym. hydrogenation using rhodium-(R,R)- or -(S,S)-EtDuPhos(COD)OTs complex as chiral catalysts, to give (+)-(S)- or (-)-(R)-2,3-(MeO)2C6H3CH2CH2CH(NHCO2Me)CO2H with 92% and 95% ee, resp. Cyclization of the acids to give tetralones, redn. of carbonyl, N-methylation, hydrolysis, O-demethylation, and esterification with isobutyroyl chloride in CF3CO2H, gave (+)-(R)- and (-)-(S)-II.HCl with approx. 95% ee in both cases. In several receptor assays, (-)-(S)-III showed 20 times the affinity for D2 dopaminergic receptors, and 10 times the affinity for .alpha.2 receptors, when compared to its enantiomer (+)-(R)-III, while showing similar activity at D1, .alpha.1, .beta.1, and .beta.2 receptors. This difference in activity was reflected in animal expts. using spontaneously hypertensive rats.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD

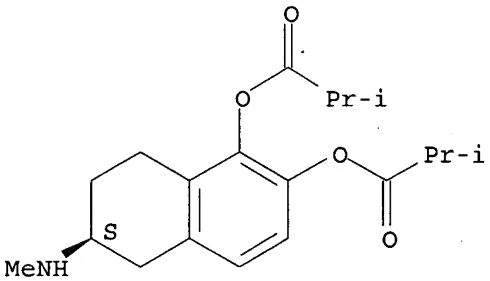
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 373361-89-8 REGISTRY
CN Butanedioic acid, 2,3-bis(benzoyloxy)-, (2S,3S)-, compd. with (6S)-5,6,7,8-tetrahydro-6-(methylamino)-1,2-naphthalenediyl bis(2-methylpropanoate) (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Propanoic acid, 2-methyl-, (6S)-5,6,7,8-tetrahydro-6-(methylamino)-1,2-naphthalenediyl ester, (2S,3S)-2,3-bis(benzoyloxy)butanedioate (1:1) (9CI)
OTHER NAMES:
CN (-)-(S)-5,6-Diisobutyroyloxy-2-methylaminotetralin (+)-D-dibenzoyltartrate
FS STEREOSEARCH
MF C19 H27 N O4 . C18 H14 O8
SR CA
LC STN Files: CA, CAPLUS

CM 1

CRN 146085-50-9
CMF C19 H27 N O4

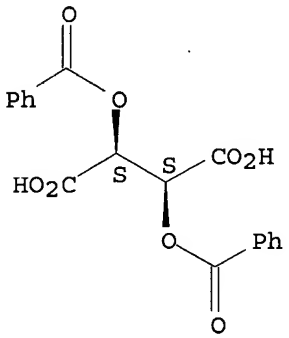
Absolute stereochemistry. Rotation (-).



CM 2

CRN 17026-42-5
CMF C18 H14 O8

Absolute stereochemistry. Rotation (+).



1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

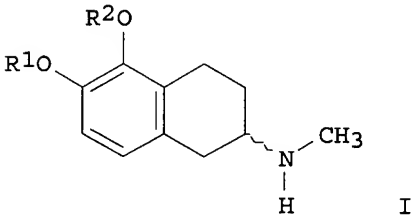
REFERENCE 1

AN 135:357780 CA
TI Optically active 2-aminotetralin derivatives, the processes for the preparation thereof, and the therapeutic use of pharmaceutical compositions containing them as antihypertensives, etc.
IN Amari, Gabriele; Del Canale, Maurizio; Razzetti, Roberta; Monici Preti, Pier Alessandro; Rondelli, Ivano

PA Chiesi Farmaceutici S.p.A., Italy
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001085668	A1	20011115	WO 2001-EP5212	20010508
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IT 2000MI1053	A1	20011112	IT 2000-MI1053	20000512
EP 1280759	A1	20030205	EP 2001-940415	20010508
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NO 2002005393	A	20030113	NO 2002-5393	20021111
PRAI IT 2000-MI1053	20000512			
WO 2001-EP5212	20010508			

GI



I

AB The invention concerns the use of the optically active forms of 5,6-dihydroxy-2-methylaminotetralin and their acyl esters, namely I [R1, R2 = H, C1-4 acyl], and their pharmaceutically acceptable salts, as medicaments. Also disclosed are a process for prepn. of I, and the use of I in pharmaceutical compns. Examples illustrate the prepn. of (+)- and (-)-I [R1 = R2 = isobutyroyl (II)] and the biol. activity of (+)- and (-)-I [R1 = R2 = H (III)]. For instance, (.+-.)-II.HCl was resolved using (-)-L- and (+)-D-dibenzoyltartaric acids to give (+)-(R)- and (-)-(S)-II.HCl with > 99% enantiomeric excess (ee) in both cases. Alternatively, 3-methoxycarbonylamino-5-(2,3-dimethoxyphenyl)-2,5-dihydrofuran-2-one underwent asym. hydrogenation using rhodium-(R,R)- or -(S,S)-EtDuPhos(COD)OTs complex as chiral catalysts, to give (+)-(S)- or (-)-(R)-2,3-(MeO)2C6H3CH2CH2CH(NHCO2Me)CO2H with 92% and 95% ee, resp. Cyclization of the acids to give tetralones, redn. of carbonyl, N-methylation, hydrolysis, O-demethylation, and esterification with isobutyroyl chloride in CF3CO2H, gave (+)-(R)- and (-)-(S)-II.HCl with approx. 95% ee in both cases. In several receptor assays, (-)-(S)-III showed 20 times the affinity for D2 dopaminergic receptors, and 10 times the affinity for .alpha.2 receptors, when compared to its enantiomer (+)-(R)-III, while showing similar activity at D1, .alpha.1, .beta.1, and .beta.2 receptors. This difference in activity was reflected in animal expts. using spontaneously hypertensive rats.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

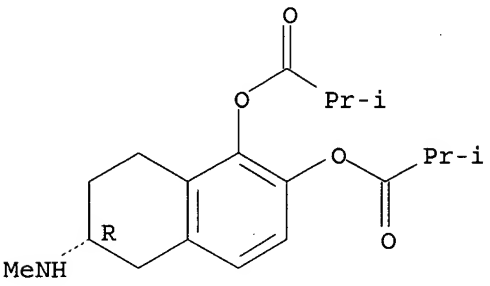
L2 ANSWER 3 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 373361-88-7 REGISTRY
CN Butanedioic acid, 2,3-bis(benzoyloxy)-, (2R,3R)-, compd. with (6R)-5,6,7,8-tetrahydro-6-(methylamino)-1,2-naphthalenediyl bis(2-methylpropanoate) (1:1) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:
CN Propanoic acid, 2-methyl-, (6R)-5,6,7,8-tetrahydro-6-(methylamino)-1,2-naphthalenediyl ester, (2R,3R)-2,3-bis(benzoyloxy)butanedioate (1:1) (9CI)
OTHER NAMES:
CN (+)-(R)-5,6-Diisobutyroyloxy-2-methylaminotetralin (-)-L-dibenzoyltartrate
FS STEREOSEARCH
MF C19 H27 N O4 . C18 H14 O8
SR CA
LC STN Files: CA, CAPLUS

CM 1

CRN 146085-52-1
CMF C19 H27 N O4

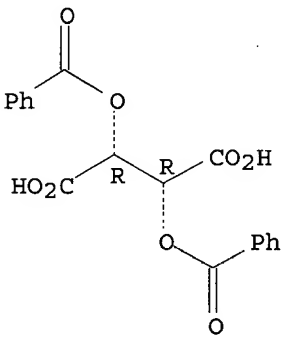
Absolute stereochemistry. Rotation (+).



CM 2

CRN 2743-38-6
CMF C18 H14 O8

Absolute stereochemistry.



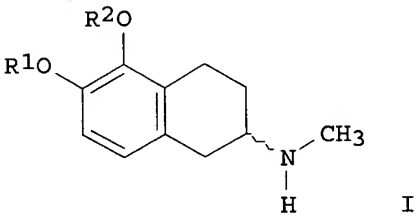
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1

AN 135:357780 CA
TI Optically active 2-aminotetralin derivatives, the processes for the preparation thereof, and the therapeutic use of pharmaceutical compositions containing them as antihypertensives, etc.
IN Amari, Gabriele; Del Canale, Maurizio; Razzetti, Roberta; Monici Preti, Pier Alessandro; Rondelli, Ivano
PA Chiesi Farmaceutici S.p.A., Italy
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE

PI	WO 2001085668	A1	20011115	WO 2001-EP5212	20010508
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	IT 2000MI1053	A1	20011112	IT 2000-MI1053	20000512
	EP 1280759	A1	20030205	EP 2001-940415	20010508
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	NO 2002005393	A	20030113	NO 2002-5393	20021111
PRAI	IT 2000-MI1053	20000512			
	WO 2001-EP5212	20010508			

GI

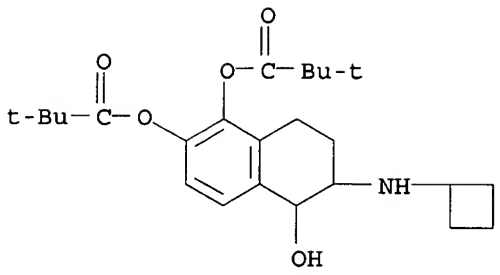


I

AB The invention concerns the use of the optically active forms of 5,6-dihydroxy-2-methylaminotetralin and their acyl esters, namely I [R1, R2 = H, C1-4 acyl], and their pharmaceutically acceptable salts, as medicaments. Also disclosed are a process for prepn. of I, and the use of I in pharmaceutical compns. Examples illustrate the prepn. of (+)- and (-)-I [R1 = R2 = isobutyroyl (II)] and the biol. activity of (+)- and (-)-I [R1 = R2 = H (III)]. For instance, (.+-.)-II.HCl was resolved using (-)-L- and (+)-D-dibenzoyltartaric acids to give (+)-(R)- and (-)-(S)-II.HCl with > 99% enantiomeric excess (ee) in both cases. Alternatively, 3-methoxycarbonylamino-5-(2,3-dimethoxyphenyl)-2,5-dihydrofuran-2-one underwent asym. hydrogenation using rhodium-(R,R)- or -(S,S)-EtDuPhos(COD)OTs complex as chiral catalysts, to give (+)-(S)- or (-)-(R)-2,3-(MeO)2C6H3CH2CH2CH(NHCO2Me)CO2H with 92% and 95% ee, resp. Cyclization of the acids to give tetralones, redn. of carbonyl, N-methylation, hydrolysis, O-demethylation, and esterification with isobutyroyl chloride in CF3CO2H, gave (+)-(R)- and (-)-(S)-II.HCl with approx. 95% ee in both cases. In several receptor assays, (-)-(S)-III showed 20 times the affinity for D2 dopaminergic receptors, and 10 times the affinity for .alpha.2 receptors, when compared to its enantiomer (+)-(R)-III, while showing similar activity at D1, .alpha.1, .beta.1, and .beta.2 receptors. This difference in activity was reflected in animal expts. using spontaneously hypertensive rats.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 156277-61-1 REGISTRY
CN Propanoic acid, 2,2-dimethyl-, 6-(cyclobutylamino)-5,6,7,8-tetrahydro-5-hydroxy-1,2-naphthalenediyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C24 H35 N O5
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

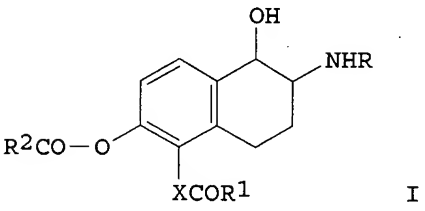
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1

AN 121:91851 CA
TI .beta.2-Adrenergic agonists and use thereof in the treatment of glaucoma
IN York, Billie M.; Kyba, Evan P.
PA Alcon Laboratories, Inc., USA
SO U.S., 4 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5314916	A	19940524	US 1993-49462	19930419
PRAI	US 1993-49462		19930419		

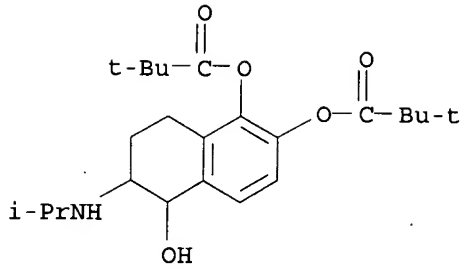
GI



I

AB Ophthalmic compns. for controlling intraocular pressure comprise tetrahydronaphthalene derivs.(I; X = O, NH; R, R1, R2 = alkyl, cycloalkyl) having .beta.2 adrenergic agonist activity. The compds. are believed to be useful in controlling intraocular pressure by increasing the outflow of aq. humor. The compds. are considered to be less likely to cause cardiovascular side effects and various other side effects assocd. with stimulation of .beta.1 receptors, relative to epinephrine.

L2 ANSWER 5 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 156277-60-0 REGISTRY
CN Propanoic acid, 2,2-dimethyl-, 5,6,7,8-tetrahydro-5-hydroxy-6-[(1-methylethyl)amino]-1,2-naphthalenediyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H35 N O5
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

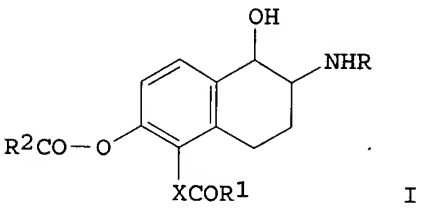
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1

AN 121:91851 CA
TI .beta.2-Adrenergic agonists and use thereof in the treatment of glaucoma
IN York, Billie M.; Kyba, Evan P.
PA Alcon Laboratories, Inc., USA
SO U.S., 4 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5314916	A	19940524	US 1993-49462	19930419
PRAI	US 1993-49462		19930419		

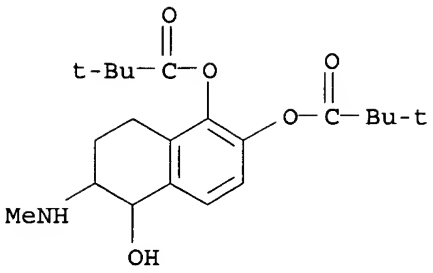
GI



I

AB Ophthalmic compns. for controlling intraocular pressure comprise tetrahydronaphthalene derivs. (I; X = O, NH; R, R1, R2 = alkyl, cycloalkyl) having .beta.2 adrenergic agonist activity. The compds. are believed to be useful in controlling intraocular pressure by increasing the outflow of aq. humor. The compds. are considered to be less likely to cause cardiovascular side effects and various other side effects assocd. with stimulation of .beta.1 receptors, relative to epinephrine.

L2 ANSWER 6 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 156277-59-7 REGISTRY
CN Propanoic acid, 2,2-dimethyl-, 5,6,7,8-tetrahydro-5-hydroxy-6-(methylamino)-1,2-naphthalenediyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C21 H31 N O5
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

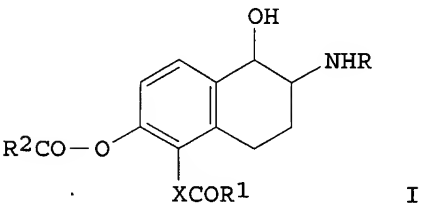
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1

AN 121:91851 CA
TI .beta.2-Adrenergic agonists and use thereof in the treatment of glaucoma
IN York, Billie M.; Kyba, Evan P.
PA Alcon Laboratories, Inc., USA
SO U.S., 4 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5314916	A	19940524	US 1993-49462	19930419
PRAI	US 1993-49462		19930419		

GI



I

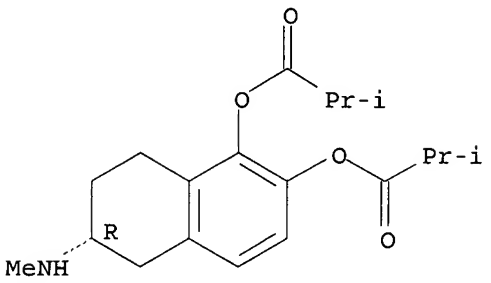
AB Ophthalmic compns. for controlling intraocular pressure comprise tetrahydronaphthalene derivs.(I; X = O, NH; R, R1, R2 = alkyl, cycloalkyl) having .beta.2 adrenergic agonist activity. The compds. are believed to be useful in controlling intraocular pressure by increasing the outflow of aq. humor. The compds. are considered to be less likely to cause cardiovascular side effects and various other side effects assocd. with stimulation of .beta.1 receptors, relative to epinephrine.

L2 ANSWER 7 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 146085-53-2 REGISTRY
CN .gamma.-Cyclodextrin, compd. with (R)-5,6,7,8-tetrahydro-6-(methylamino)-1,2-naphthalenediyl bis(2-methylpropanoate) (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2,4,7,9,12,14,17,19,22,24,27,29,32,34,37,39-Hexadecaoxanonacyclo[36.2.2.23,6.28,11.213,16.218,21.223,26.228,31.233,36]hexapentacontane, .gamma.-cyclodextrin deriv.
CN Propanoic acid, 2-methyl-, 5,6,7,8-tetrahydro-6-(methylamino)-1,2-naphthalenediyl ester, (R)-, compd. with .gamma.-cyclodextrin (1:1) (9CI)
FS STEREOSEARCH
MF C48 H80 O40 . C19 H27 N O4
SR CA
LC STN Files: CA, CAPLUS

CM 1

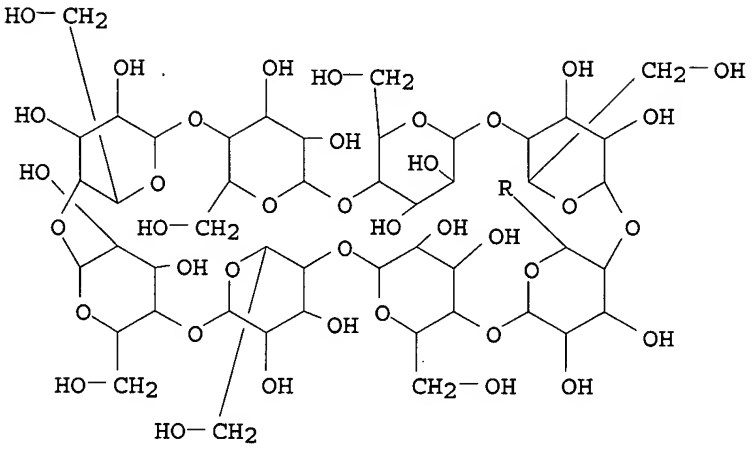
CRN 146085-52-1
CMF C19 H27 N O4

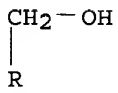
Absolute stereochemistry. Rotation (+).



CM 2

CRN 17465-86-0
CMF C48 H80 O40

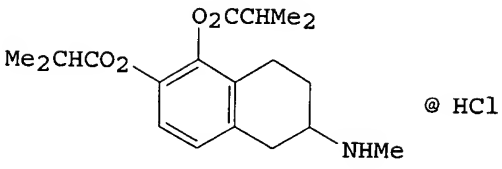




1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1

AN 118:154695 CA
TI Application of .gamma.-cyclodextrin to enantiomeric purity determination of a new 2-aminotetralin derivative by proton NMR spectroscopy
AU Redenti, Enrico; Fronza, Giovanni; Bovis, Giovanni; Ventura, Paolo
CS Chem. Biopharm. Dep., Chiesi Farm. S.p.A., Parma, I-43100, Italy
SO Chirality (1992), 4(6), 404-5
CODEN: CHRLEP; ISSN: 0899-0042
DT Journal
LA English
GI

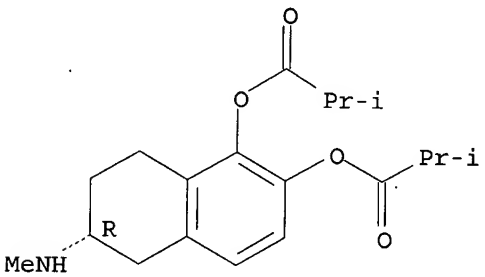


I

AB .gamma.-Cyclodextrin was used to perform chiral discrimination of (.+-.)-5,6-diisobutyroyl-2-methylaminotetralin-HCl (I) by 1H-NMR; the 95% enantiomeric excess of the (-)-isomer was detd. successfully.

L2 ANSWER 8 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 146085-52-1 REGISTRY
CN Propanoic acid, 2-methyl-, (6R)-5,6,7,8-tetrahydro-6-(methylamino)-1,2-naphthalenediyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Propanoic acid, 2-methyl-, 5,6,7,8-tetrahydro-6-(methylamino)-1,2-naphthalenediyl ester, (R)-
OTHER NAMES:
CN (+)-(R)-5,6-Diisobutyryloxy-2-methylaminotetralin
CN CHF 1800
FS STEREOSEARCH
MF C19 H27 N O4
CI COM
SR CA
LC STN Files: CA, CAPLUS, DRUGPAT, DRUGUPDATES

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1957 TO DATE)
3 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1

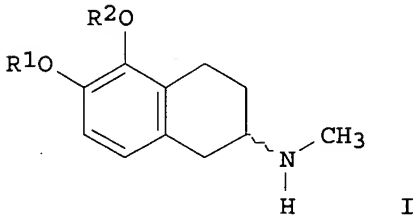
AN 135:357780 CA
TI Optically active 2-aminotetralin derivatives, the processes for the preparation thereof, and the therapeutic use of pharmaceutical compositions containing them as antihypertensives, etc.
IN Amari, Gabriele; Del Canale, Maurizio; Razzetti, Roberta; Monici Preti, Pier Alessandro; Rondelli, Ivano
PA Chiesi Farmaceutici S.p.A., Italy
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001085668	A1	20011115	WO 2001-EP5212	20010508

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

IT 2000MI1053 A1 20011112 IT 2000-MI1053 20000512
EP 1280759 A1 20030205 EP 2001-940415 20010508
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
NO 2002005393 A 20030113 NO 2002-5393 20021111
PRAI IT 2000-MI1053 20000512
WO 2001-EP5212 20010508
GI



I

AB The invention concerns the use of the optically active forms of 5,6-dihydroxy-2-methylaminotetralin and their acyl esters, namely I [R1, R2 = H, C1-4 acyl], and their pharmaceutically acceptable salts, as medicaments. Also disclosed are a process for prepn. of I, and the use of I in pharmaceutical compns. Examples illustrate the prepn. of (+)- and (-)-I [R1 = R2 = isobutyroyl (II)] and the biol. activity of (+)- and (-)-I [R1 = R2 = H (III)]. For instance, (.+-.)-II.HCl was resolved using (-)-L- and (+)-D-dibenzoyltartaric acids to give (+)-(R)- and (-)-(S)-II.HCl with > 99% enantiomeric excess (ee) in both cases. Alternatively, 3-methoxycarbonylamino-5-(2,3-dimethoxyphenyl)-2,5-dihydrofuran-2-one underwent asym. hydrogenation using rhodium-(R,R)- or -(S,S)-EtDuPhos(COD)OTs complex as chiral catalysts, to give (+)-(S)- or (-)-(R)-2,3-(MeO)2C6H3CH2CH2CH(NHCO2Me)CO2H with 92% and 95% ee, resp. Cyclization of the acids to give tetralones, redn. of carbonyl, N-methylation, hydrolysis, O-demethylation, and esterification with isobutyroyl chloride in CF3CO2H, gave (+)-(R)- and (-)-(S)-II.HCl with approx. 95% ee in both cases. In several receptor assays, (-)-(S)-III showed 20 times the affinity for D2 dopaminergic receptors, and 10 times the affinity for .alpha.2 receptors, when compared to its enantiomer (+)-(R)-III, while showing similar activity at D1, .alpha.1, .beta.1, and .beta.2 receptors. This difference in activity was reflected in animal expts. using spontaneously hypertensive rats.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

REFERENCE 2

AN 126:220252 CA
TI New method for the resolution of the enantiomers of 5,6-dihydroxy-2-methyl-aminotetralin by selective derivatization and HPLC. [Erratum to document cited in CA125:316086]
AU Rondelli, Ivano; Corsaletti, Roberto; Redenti, Enrico; Acerbi, Daniela; Delcanale, Maurizio; Amari, Gabriele; Ventura, Paolo
CS Chemical Biopharmaceutical Direction, Parma, Italy
SO Chirality (1997), 9(1), 89
CODEN: CHRLEP; ISSN: 0899-0042
PB Wiley-Liss
DT Journal
LA English
AB The errors were not reflected in the abstr. or the index entries.

REFERENCE 3

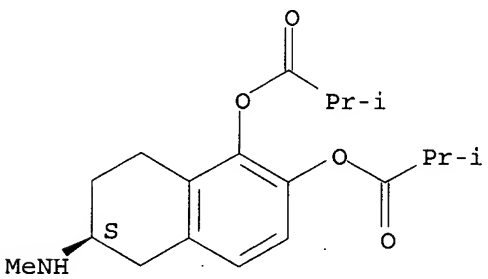
AN 125:316086 CA
TI New method for the resolution of the enantiomers of 5,6-dihydroxy-2-methyl-aminotetralin by selective derivatization and HPLC analysis: application to biological fluids
AU Rondelli, Ivano; Corsaletti, Roberto; Redenti, Enrico; Acerbi, Daniela; Delcanale, Maurizio; Amari, Gabriele; Ventura, Paolo
CS Chemical Biopharmaceutical Direction, Chiesi Farmaceutici S.p.A., Parma, Italy
SO Chirality (1996), 8(5), 381-389
CODEN: CHRLEP; ISSN: 0899-0042
PB Wiley-Liss
DT Journal
LA English
AB A new chiral derivatization procedure for the HPLC resoln. of chiral catecholamines and structurally related compds. is described. The homochiral reagent, (+)-(R)-1-phenylethyl isocyanate (RPEIC), was added to sep. and quantitate the enantiomers of rac-5,6-dihydroxy-2-methyl-aminotetralin, the main metabolite of rac-5,6-diisobutyryl-2-methyl-aminotetralin, a potent dopamine agonist, by reversed-phase HPLC anal. To avoid catecholamine degrdn. in the basic reaction medium and to obtain the selective and quant. derivatization of the amino group of the compd., the reversible complex formation between diphenylborinic acid (DPBA) and the catechol group, in alk. medium, was performed before homochiral isocyanate addn. The RPEIC derivatization was completed in 30 min and then the DPBA complex was dissocd. by adding dil. acid. The structure of intermediates and urea derivs. was confirmed by mass spectrometry. The use of an electrochem. detector, operating in redox mode, allowed HPLC quantitation of enantiomers at the nanogram level in plasma and urine. The derivatization procedure is also suitable for other catecholamine-related compds.

L2 ANSWER 9 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 146085-51-0 REGISTRY
CN .gamma.-Cyclodextrin, compd. with (S)-5,6,7,8-tetrahydro-6-(methylamino)-1,2-naphthalenediyl bis(2-methylpropanoate) (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2,4,7,9,12,14,17,19,22,24,27,29,32,34,37,39-Hexadecaoxanonacyclo[36.2.2.23,6.28,11.213,16.218,21.223,26.228,31.233,36]hexapentacontane, .gamma.-cyclodextrin deriv.
CN Propanoic acid, 2-methyl-, 5,6,7,8-tetrahydro-6-(methylamino)-1,2-naphthalenediyl ester, (S)-, compd. with .gamma.-cyclodextrin (1:1) (9CI)
FS STEREOSEARCH
MF C48 H80 O40 . C19 H27 N O4
SR CA
LC STN Files: CA, CAPLUS

CM 1

CRN 146085-50-9
CMF C19 H27 N O4

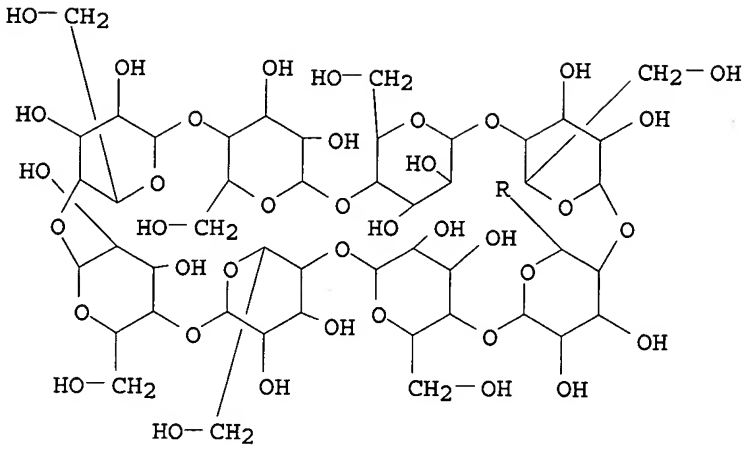
Absolute stereochemistry. Rotation (-).

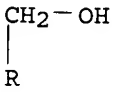


102

CM 2

CRN 17465-86-0
CMF C48 H80 O40

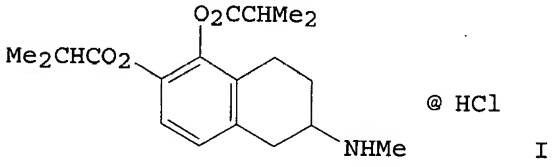




1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1

AN 118:154695 CA
TI Application of .gamma.-cyclodextrin to enantiomeric purity determination of a new 2-aminotetralin derivative by proton NMR spectroscopy
AU Redenti, Enrico; Fronza, Giovanni; Bovis, Giovanni; Ventura, Paolo
CS Chem. Biopharm. Dep., Chiesi Farm. S.p.A., Parma, I-43100, Italy
SO Chirality (1992), 4(6), 404-5
CODEN: CHRLEP; ISSN: 0899-0042
DT Journal
LA English
GI



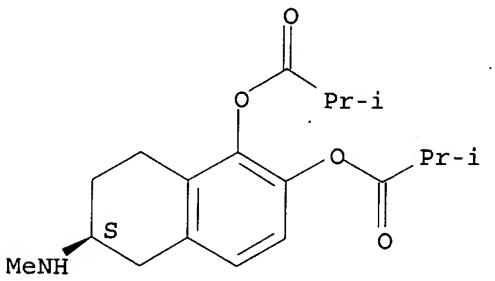
I

AB .gamma.-Cyclodextrin was used to perform chiral discrimination of (.+-.)-5,6-diisobutyroyl-2-methylaminotetralin-HCl (I) by 1H-NMR; the 95% enantiomeric excess of the (-)-isomer was detd. successfully.

L2 ANSWER 10 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 146085-50-9 REGISTRY
CN Propanoic acid, 2-methyl-, 5,6,7,8-tetrahydro-6-(methylamino)-1,2-naphthalenediyl ester, (6S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Propanoic acid, 2-methyl-, 5,6,7,8-tetrahydro-6-(methylamino)-1,2-naphthalenediyl ester, (S)-
OTHER NAMES:
CN (-)-(S)-5,6-diisobutyroyloxy-2-methylaminotetralin
CN CHF 1810
FS STEREOSEARCH

MF C19 H27 N O4
CI COM
SR CA
LC STN Files: CA, CAPLUS, DRUGPAT, DRUGUPDATES

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

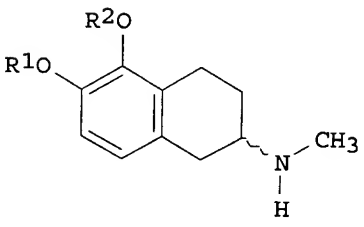
4 REFERENCES IN FILE CA (1957 TO DATE)
4 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1

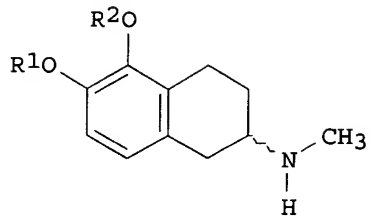
AN 135:357780 CA
TI Optically active 2-aminotetralin derivatives, the processes for the preparation thereof, and the therapeutic use of pharmaceutical compositions containing them as antihypertensives, etc.
IN Amari, Gabriele; Del Canale, Maurizio; Razzetti, Roberta; Monici Preti, Pier Alessandro; Rondelli, Ivano
PA Chiesi Farmaceutici S.p.A., Italy
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001085668	A1	20011115	WO 2001-EP5212	20010508
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	IT 2000MI1053	A1	20011112	IT 2000-MI1053	20000512
	EP 1280759	A1	20030205	EP 2001-940415	20010508
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	NO 2002005393	A	20030113	NO 2002-5393	20021111
PRAI	IT 2000-MI1053	20000512			
	WO 2001-EP5212	20010508			

GI



I



I

AB The invention concerns the use of the optically active forms of 5,6-dihydroxy-2-methylaminotetralin and their acyl esters, namely I [R1, R2 = H, C1-4 acyl], and their pharmaceutically acceptable salts, as medicaments. Also disclosed are a process for prepn. of I, and the use of I in pharmaceutical compns. Examples illustrate the prepn. of (+)- and (-)-I [R1 = R2 = isobutyroyl (II)] and the biol. activity of (+)- and (-)-I [R1 = R2 = H (III)]. For instance, (.+-.)-II.HCl was resolved using (-)-L- and (+)-D-dibenzoyltartaric acids to give (+)-(R)- and (-)-(S)-II.HCl with > 99% enantiomeric excess (ee) in both cases. Alternatively, 3-methoxycarbonylamino-5-(2,3-dimethoxyphenyl)-2,5-dihydrofuran-2-one underwent asym. hydrogenation using rhodium-(R,R)- or -(S,S)-EtDuPhos(COD)OTs complex as chiral catalysts, to give (+)-(S)- or (-)-(R)-2,3-(MeO)2C6H3CH2CH2CH(NHCO2Me)CO2H with 92% and 95% ee, resp. Cyclization of the acids to give tetralones, redn. of carbonyl, N-methylation, hydrolysis, O-demethylation, and esterification with isobutyroyl chloride in CF3CO2H, gave (+)-(R)- and (-)-(S)-II.HCl with approx. 95% ee in both cases. In several receptor assays, (-)-(S)-III showed 20 times the affinity for D2 dopaminergic receptors, and 10 times the affinity for .alpha.2 receptors, when compared to its enantiomer (+)-(R)-III, while showing similar activity at D1, .alpha.1, .beta.1, and .beta.2 receptors. This difference in activity was reflected in animal expts. using spontaneously hypertensive rats.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

REFERENCE 2

AN 134:125975 CA
TI 2-Aminotetralin derivatives for the therapy of glaucoma
IN Bongrani, Stefano; Razzetti, Roberta; Chiesi, Paolo
PA Chiesi Farmaceutici S.P.A., Italy
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001008667	A2	20010208	WO 2000-EP7184	20000726
	WO 2001008667	A3	20010607		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	IT 99MI1713	A1	20010130	IT 1999-MI1713	19990730
	EP 1200079	A2	20020502	EP 2000-956296	20000726
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	JP 2003505499	T2	20030212	JP 2001-513397	20000726
	NO 2002000475	A	20020313	NO 2002-475	20020129
PRAI	IT 1999-MI1713	19990730			
	WO 2000-EP7184	20000726			

AB Disclosed is the use of racemic or optically active compds. of

5,6-diisobutyroyloxy-2-methylaminotetralin, 5,6-diisobutyroyloxy-2-aminotetralin, and salts thereof for the prepn. of pharmaceutical compns. for the therapy of ophthalmic disorders. Intraocular pressure-lowering activities of CHF 1035 were tested with rabbits.

REFERENCE 3

AN 126:220252 CA
TI New method for the resolution of the enantiomers of 5,6-dihydroxy-2-methyl-aminotetralin by selective derivatization and HPLC. [Erratum to document cited in CA125:316086]
AU Rondelli, Ivano; Corsaletti, Roberto; Redenti, Enrico; Acerbi, Daniela; Delcanale, Maurizio; Amari, Gabriele; Ventura, Paolo
CS Chemical Biopharmaceutical Direction, Parma, Italy
SO Chirality (1997), 9(1), 89
CODEN: CHRLEP; ISSN: 0899-0042
PB Wiley-Liss
DT Journal
LA English
AB The errors were not reflected in the abstr. or the index entries.

REFERENCE 4

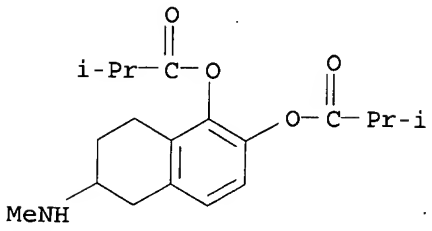
AN 125:316086 CA
TI New method for the resolution of the enantiomers of 5,6-dihydroxy-2-methyl-aminotetralin by selective derivatization and HPLC analysis: application to biological fluids
AU Rondelli, Ivano; Corsaletti, Roberto; Redenti, Enrico; Acerbi, Daniela; Delcanale, Maurizio; Amari, Gabriele; Ventura, Paolo
CS Chemical Biopharmaceutical Direction, Chiesi Farmaceutici S.p.A., Parma, Italy
SO Chirality (1996), 8(5), 381-389
CODEN: CHRLEP; ISSN: 0899-0042
PB Wiley-Liss
DT Journal
LA English
AB A new chiral derivatization procedure for the HPLC resoln. of chiral catecholamines and structurally related compds. is described. The homochiral reagent, (+)-(R)-1-phenylethyl isocyanate (RPEIC), was added to sep. and quantitate the enantiomers of rac-5,6-dihydroxy-2-methyl-aminotetralin, the main metabolite of rac-5,6-diisobutyryl-2-methyl-aminotetralin, a potent dopamine agonist, by reversed-phase HPLC anal. To avoid catecholamine degrdn. in the basic reaction medium and to obtain the selective and quant. derivatization of the amino group of the compd., the reversible complex formation between diphenylborinic acid (DPBA) and the catechol group, in alk. medium, was performed before homochiral isocyanate addn. The RPEIC derivatization was completed in 30 min and then the DPBA complex was dissocd. by adding dil. acid. The structure of intermediates and urea derivs. was confirmed by mass spectrometry. The use of an electrochem. detector, operating in redox mode, allowed HPLC quantitation of enantiomers at the nanogram level in plasma and urine. The derivatization procedure is also suitable for other catecholamine-related compds.

L2 ANSWER 11 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 146085-49-6 REGISTRY
CN .gamma.-Cyclodextrin, compd. with 5,6,7,8-tetrahydro-6-(methylamino)-1,2-naphthalenediyl bis(2-methylpropanoate) (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN .gamma.-Cyclodextrin, compd. with (.+-.)-5,6,7,8-tetrahydro-6-(methylamino)-1,2-naphthalenediyl bis(2-methylpropanoate) (1:1)
CN 2,4,7,9,12,14,17,19,22,24,27,29,32,34,37,39-Hexadecaoxanonacyclo[36.2.2.23,6.28,11.213,16.218,21.223,26.228,31.233,36]hexapentacontane, .gamma.-cyclodextrin deriv.
CN Propanoic acid, 2-methyl-, 5,6,7,8-tetrahydro-6-(methylamino)-1,2-naphthalenediyl ester, (.+-.)-, compd. with .gamma.-cyclodextrin (1:1)
CN Propanoic acid, 2-methyl-, 5,6,7,8-tetrahydro-6-(methylamino)-1,2-naphthalenediyl ester, compd. with .gamma.-cyclodextrin (1:1) (9CI)
MF C48 H80 O40 . C19 H27 N O4

SR CA
LC STN Files: CA, CAPLUS

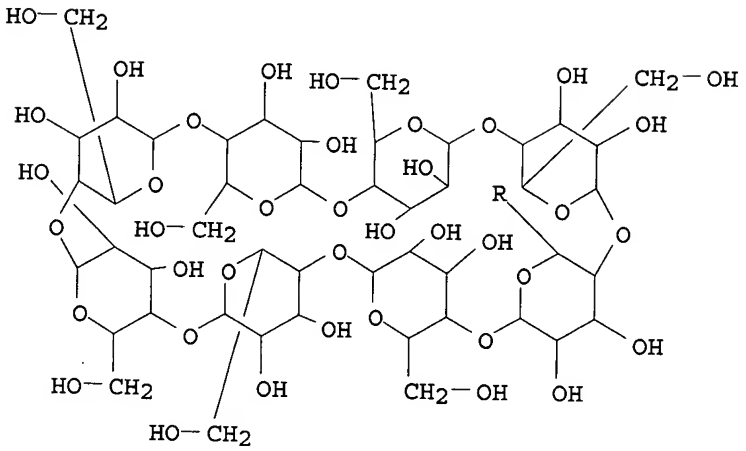
CM 1

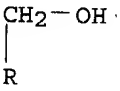
CRN 90060-42-7
CMF C19 H27 N O4



CM 2

CRN 17465-86-0
CMF C48 H80 O40

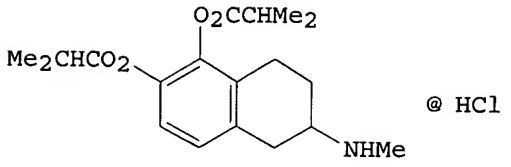




1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1

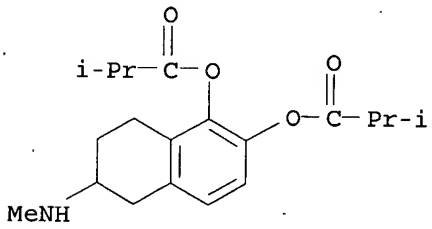
AN 118:154695 CA
TI Application of .gamma.-cyclodextrin to enantiomeric purity determination of a new 2-aminotetralin derivative by proton NMR spectroscopy
AU Redenti, Enrico; Fronza, Giovanni; Bovis, Giovanni; Ventura, Paolo
CS Chem. Biopharm. Dep., Chiesi Farm. S.p.A., Parma, I-43100, Italy
SO Chirality (1992), 4(6), 404-5
CODEN: CHRLEP; ISSN: 0899-0042
DT Journal
LA English
GI



I

AB .gamma.-Cyclodextrin was used to perform chiral discrimination of (.+-.)-5,6-diisobutyroyl-2-methylaminotetralin-HCl (I) by 1H-NMR; the 95% enantiomeric excess of the (-)-isomer was detd. successfully.

L2 ANSWER 12 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 138531-51-8 REGISTRY
CN Propanoic acid, 2-methyl-, 5,6,7,8-tetrahydro-6-(methylamino)-1,2-naphthalenediyl ester, hydrochloride (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Propanoic acid, 2-methyl-, 5,6,7,8-tetrahydro-6-(methylamino)-1,2-naphthalenediyl ester, hydrochloride, (.+-.)-
OTHER NAMES:
CN CHF 1035
CN Nolomirole hydrochloride
MF C19 H27 N O4 . Cl H
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, BIOSIS, CA, CAPLUS, DRUGPAT, DRUGUPDATES, IPA, PHAR, SYNTHLINE, TOXCENTER, USPATFULL
CRN (90060-42-7)



● HCl

11 REFERENCES IN FILE CA (1957 TO DATE)
11 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1

AN 138:16518 CA
TI Vibrational study of polymorphism of tetralin derivative for treatment of cardiovascular diseases
AU Taddei, Paola; Torreggiani, Armida; Fini, Giancarlo
CS Dipartimento di Biochimica G. Moruzzi, Sezione di Chimica e Propedeutic Biochimica, University of Bologna, Bologna, 40126, Italy
SO Biopolymers (2002), Volume Date 2001-2002, 61(3), 289-293
CODEN: BIPMAA; ISSN: 0006-3525
PB John Wiley & Sons, Inc.
DT Journal
LA English
AB Vibrational spectroscopy coupled with thermogravimetry (TG) and differential scanning calorimetry (DSC) was used to characterize racemic propanoic acid, 2-methyl-5,6,7,8-tetrahydro-6-(methylamino)-1,2-naphthalenediyl ester hydrochloride (CHF-1035), which is a new DA2 dopaminergic receptor/.alpha.2 agonist and .beta. blocker under clin. investigation for the treatment of congestive heart failure. Raman spectroscopy disclosed at least two different CHF-1035 polymorphs; the marker bands characteristic of each form were identified. The modifications undergone by the CHF-1035 drug as a consequence of grinding

and heating were investigated. Mech. and gentle thermal treatments caused a polymorphic transformation of the drug crystal form. Raman spectroscopy proved suitable for investigating the possible presence of different polymorphic forms, their relative stability, and interconversion tendency in relation to industrial manufg. processes undergone by the drug (i.e., grinding, compression, and heating).

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

REFERENCE 2

AN 137:134225 CA
TI Nolomirole hydrochloride: treatment of heart failure dopamine D2 agonist .alpha.2-adrenoreceptor agonist CHF-1035
AU Mealy, N. E.; Leeson, P. A.; Bayes, M.; Castaner, J.
CS Prous Science, Barcelona, 08080, Spain
SO Drugs of the Future (2001), 26(11), 1046-1051
CODEN: DRFUD4; ISSN: 0377-8282
PB Prous Science
DT Journal; General Review
LA English
AB A review describes the synthesis, pharmacol. actions, metab., and clin. studies of nolomirole hydrochloride. Nolomirole hydrochloride is a recently developed, orally active dopamine agonist that activates prejunctional dopamine D2 receptors and .alpha.-adrenoreceptors. The drug is rapidly hydrolyzed to its active metabolite CHF-1024 following oral administration.

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

REFERENCE 3

AN 137:68157 CA
TI Inhalant compositions containing anticholinergics and dopamine agonists
IN Pairet, Michel; Pieper, Michael Paul; Meade, Christopher John Montague
PA Boehringer Ingelheim Pharma Kg, Germany
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002049624	A2	20020627	WO 2001-EP14568	20011212
	WO 2002049624	A3	20020919		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	DE 10063957	A1	20020627	DE 2000-10063957	20001220
	AU 2002035767	A5	20020701	AU 2002-35767	20011212
	US 2002122773	A1	20020905	US 2001-27662	20011220
PRAI	DE 2000-10063957		20001220		
	US 2000-257221P		20001221		
	WO 2001-EP14568		20011212		

AB The invention relates to novel pharmaceutical compns. based on anticholinergic agents and dopamine agonists, a method for the prodn. of the compns. and the use of the same for the treatment of respiratory tract diseases. Thus an inhalation powder contained per capsule (.mu.g): tiotropium bromide 21.7; viozan 270; lactose 4708.3.

REFERENCE 4

AN 137:28116 CA
TI Autonomic and hemodynamic effects of a new selective dopamine agonist, CHF 1035, in patients with chronic heart failure
AU Tjeerdsma, Geert; van Wijk, Leen M.; Molhoek, G. Peter; Boomsma, Frans; Haaksma, Jaap; van Veldhuisen, Dirk J.
CS Department of Cardiology/Thoraxcenter, University Hospital Groningen, Groningen, 9700 RB, Neth.
SO Cardiovascular Drugs and Therapy (2001), 15(2), 139-145
CODEN: CDTHET; ISSN: 0920-3206
PB Kluwer Academic Publishers
DT Journal
LA English
AB Dopamine agonists have been studied in chronic heart failure, but earlier reports with non-selective compds. demonstrated unfavorable long-term effects. CHF 1035 is an orally active, new selective dopamine agonist, primarily activating DA2- and .alpha.2 receptors, thereby inhibiting norepinephrine release, which may be beneficial in heart failure. The authors conducted a double-blind, placebo-controlled comparison of CHF 1035 (10 mg/day, n = 20) and placebo (n = 9) in patients with mild to moderate chronic heart failure (left ventricular ejection fraction <0.45). Patients were clin. stable on diuretics and angiotensin-converting enzyme inhibitors. Both acute and chronic assessments were made, including plasma neurohormones and 24-h Holter monitoring for heart rate variability anal. CHF 1035 was generally well tolerated during the study. After 10 days, there were no significant changes between the groups regarding heart rate and blood pressure. Compared to placebo, plasma norepinephrine levels decreased on CHF 1035, both in the first 4 h and after 10 days ($p<0.05$ between groups). Other neurohormones (natriuretic peptides, renin, aldosterone, and endothelin) were not significantly affected. Heart rate variability parameters generally increased on CHF 1035 but were unaffected by placebo ($p<0.05$ between groups). Short-term treatment with the selective dopaminergic agonist CHF 1035 is well tolerated, reduces plasma norepinephrine concns., and increases heart rate variability in mild chronic heart failure.
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

REFERENCE 5

AN 136:284291 CA
TI Polymorphism of rac-5,6-diisobutyryloxy-2-methylamino-1,2,3,4-tetrahydro-naphthalene hydrochloride (CHF 1035). I. Thermal, spectroscopic, and X-ray diffraction properties
AU Giordano, Ferdinando; Rossi, Alessandra; Moyano, Jose Ramon; Gazzaniga, Andrea; Massarotti, Vincenzo; Bini, Marcella; Capsoni, Doretta; Peveri, Tiziana; Redenti, Enrico; Carima, Lorenza; Alberi, Massimiliano Dagli; Zanol, Margherita
CS Dipartimento Farmaceutico, University of Parma, Parma, I-43100, Italy
SO Journal of Pharmaceutical Sciences (2001), 90(8), 1154-1163
CODEN: JPMSAE; ISSN: 0022-3549
PB Wiley-Liss, Inc.
DT Journal
LA English
AB The polymorphism of rac-5,6-diisobutyryloxy-2-methylamino-1,2,3,4-tetrahydro-naphthalene hydrochloride (CHF 1035) was investigated. Three different crystal forms (Form I, Form II, and Form III) were obtained by recrystn. procedures from common org. solvents. The polymorphs were characterized by Raman and carbon-13 NMR (13C-NMR) spectroscopy, in soln. and in solid state (cross polarization-magic angle spinning), powder x-ray diffractometry, and thermal methods (DSC, hot stage microscopy, and thermogravimetry). Moreover, the diffraction patterns of Form I, collected at controlled temps., gave evidence of the presence of 2 reversible structural rearrangements at 60 and 75.degree.. These structural variations were confirmed by the results obtained by DSC and hot stage microscopy techniques. The anal. of the Raman spectra allowed the identification of peculiar absorption bands for each polymorph. Form III was the stable crystal form at room temp. as detd. by the basis of slurry conversion method.
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

REFERENCE 6

AN 136:144453 CA
TI Dopaminergic agents in heart failure: Rebirth of an old concept
AU Remme, Willem J.
CS Sticares Cardiovascular Research Foundation, Rhoon, Neth.
SO Cardiovascular Drugs and Therapy (2001), 15(2), 107-109
CODEN: CDTHET; ISSN: 0920-3206
PB Kluwer Academic Publishers
DT Journal; General Review
LA English
AB A review discusses the CHF 1035, an orally active prodrug, which after ingestion, is rapidly hydrolyzed to its active metabolite CHF 1024. The CHF 1035 is a neurohormonal antagonist with little to be expected in terms of pos. inotropism, increased heart rate or pro-arrhythmic effects, typical for .beta.1 agonists. The studies conducted by Masson et al. and the article by Tjeerdsma et al. are cited. The former study examd. the effect of different dosages CHF 1024 on cardiac remodelling, plasma neurohormones, and urinary catecholamine excretion in an animal model of pressure-overload hypertrophy, comparing it to the ACE inhibitor captopril, while the latter focused on the study on plasma neurohormones and heart rate variability anal.. Both studies indicate the potential usefulness of CHF 1035 (CHF 1024) in different, albeit related, conditions. Masson's study leads one to speculate that this drug might be useful in hypertension and other forms of pressure-overload to limit or prevent fibrosis and thereby one significant aspect of cardiac remodelling, before cardiac dysfunction or symptomatic heart failure has occurred. Tjeerdsma's study indicated that CHF 1035 in addn. to ACE inhibition decreases sympathetic tone and improves vagal activity, significant prognostic and pathophysiol. mechanisms in heart failure. These studies indicated a potentially significant role of this form of dopaminergic stimulation, one that may not result in the detrimental effects obsd. with the more hybrid compds., such as ibopamine.
RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

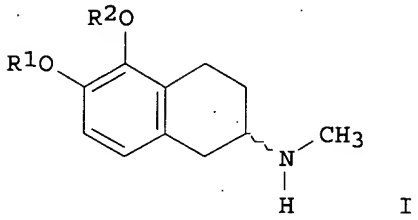
REFERENCE 7

AN 135:357780 CA
TI Optically active 2-aminotetralin derivatives, the processes for the preparation thereof, and the therapeutic use of pharmaceutical compositions containing them as antihypertensives, etc.
IN Amari, Gabriele; Del Canale, Maurizio; Razzetti, Roberta; Monici Preti, Pier Alessandro; Rondelli, Ivano
PA Chiesi Farmaceutici S.p.A., Italy
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001085668	A1	20011115	WO 2001-EP5212	20010508
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	IT 2000MI1053	A1	20011112	IT 2000-MI1053	20000512
	EP 1280759	A1	20030205	EP 2001-940415	20010508
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	NO 2002005393	A	20030113	NO 2002-5393	20021111

PRAI IT 2000-MI1053 20000512
WO 2001-EP5212 20010508

GI



I

AB The invention concerns the use of the optically active forms of 5,6-dihydroxy-2-methylaminotetralin and their acyl esters, namely I [R1, R2 = H, C1-4 acyl], and their pharmaceutically acceptable salts, as medicaments. Also disclosed are a process for prepn. of I, and the use of I in pharmaceutical compns. Examples illustrate the prepn. of (+)- and (-)-I [R1 = R2 = isobutyroyl (II)] and the biol. activity of (+)- and (-)-I [R1 = R2 = H (III)]. For instance, (.+-.)-II.HCl was resolved using (-)-L- and (+)-D-dibenzoyltartaric acids to give (+)-(R)- and (-)-(S)-II.HCl with > 99% enantiomeric excess (ee) in both cases. Alternatively, 3-methoxycarbonylamino-5-(2,3-dimethoxyphenyl)-2,5-dihydrofuran-2-one underwent asym. hydrogenation using rhodium-(R,R)- or -(S,S)-EtDuPhos(COD)OTs complex as chiral catalysts, to give (+)-(S)- or (-)-(R)-2,3-(MeO)2C6H3CH2CH2CH(NHCO2Me)CO2H with 92% and 95% ee, resp. Cyclization of the acids to give tetralones, redn. of carbonyl, N-methylation, hydrolysis, O-demethylation, and esterification with isobutyroyl chloride in CF3CO2H, gave (+)-(R)- and (-)-(S)-II.HCl with approx. 95% ee in both cases. In several receptor assays, (-)-(S)-III showed 20 times the affinity for D2 dopaminergic receptors, and 10 times the affinity for .alpha.2 receptors, when compared to its enantiomer (+)-(R)-III, while showing similar activity at D1, .alpha.1, .beta.1, and .beta.2 receptors. This difference in activity was reflected in animal expts. using spontaneously hypertensive rats.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

REFERENCE 8

AN 135:204615 CA
TI Is there a role for dopaminergics in the treatment of chronic congestive heart failure?
AU Crippa, G.
CS Hypertension Unit, Civil Hospital, Piacenza, Italy
SO Cardiovascular Pharmacotherapy, Proceedings of the International Congress on Cardiovascular Pharmacotherapy, 9th, Salvador, Brazil, Mar. 26-30, 2000 (2000), 67-72. Editor(s): Reyes, Ariel J.; Maranhao, Mario F. C. Publisher: Monduzzi Editore S.p.A., Bologna, Italy.
CODEN: 69BDEL
DT Conference; General Review
LA English
AB A review, with 19 refs. For many years, attempts have been made in search of a drug for the treatment of congestive heart failure (CHF) with vasodilatory effect, natriuretic action, inotropic properties, higher efficacy and lower toxicity than digitalis. In patients with CHF the infusion of low-dose dopamine, acting as agonist on DA1 and DA2 receptors, increases sodium excretion and cardiac output, decreases vascular resistance without changes in heart rate and O2 consumption. I.v. dopexamine, a dopamine analog, increases renal and mesenteric blood flow and in patients with heart failure its vasodilatory effect results in a redn. in filling pressure. Fenoldopam (DA1-selective agonist), and ibopamine (DA1, DA2, .beta.2 and .alpha. agonist), both orally active, have been withdrawn from the market for a possible drug-related increased mortality. The acute hemodynamic studies with CHF 1035 (a new nonselective orally active dopaminergic) have shown significant increase

in cardiac index and stroke vol. and decrease in peripheral resistance and PCWP. In 2 add-on short-term clin. studies this drug improved the clin. condition and exercise capacity in patients with CHF and results were well tolerated. The physiol. rationale and these new encouraging clin. data justify the interest to continue studying this class of drugs.

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

REFERENCE 9

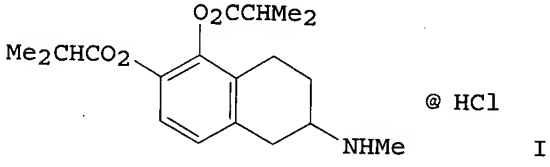
AN 134:125975 CA
TI 2-Aminotetralin derivatives for the therapy of glaucoma
IN Bongrani, Stefano; Razzetti, Roberta; Chiesi, Paolo
PA Chiesi Farmaceutici S.P.A., Italy
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001008667	A2	20010208	WO 2000-EP7184	20000726
	WO 2001008667	A3	20010607		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	IT 99MI1713	A1	20010130	IT 1999-MI1713	19990730
	EP 1200079	A2	20020502	EP 2000-956296	20000726
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	JP 2003505499	T2	20030212	JP 2001-513397	20000726
	NO 2002000475	A	20020313	NO 2002-475	20020129
PRAI	IT 1999-MI1713	19990730			
	WO 2000-EP7184	20000726			

AB Disclosed is the use of racemic or optically active compds. of 5,6-diisobutyroyloxy-2-methylaminotetralin, 5,6-diisobutyroyloxy-2-aminotetralin, and salts thereof for the prepn. of pharmaceutical compns. for the therapy of ophthalmic disorders. Intraocular pressure-lowering activities of CHF 1035 were tested with rabbits.

REFERENCE 10

AN 118:154695 CA
TI Application of .gamma.-cyclodextrin to enantiomeric purity determination of a new 2-aminotetralin derivative by proton NMR spectroscopy
AU Redenti, Enrico; Fronza, Giovanni; Bovis, Giovanni; Ventura, Paolo
CS Chem. Biopharm. Dep., Chiesi Farm. S.p.A., Parma, I-43100, Italy
SO Chirality (1992), 4(6), 404-5
CODEN: CHRLEP; ISSN: 0899-0042
DT Journal
LA English
GI

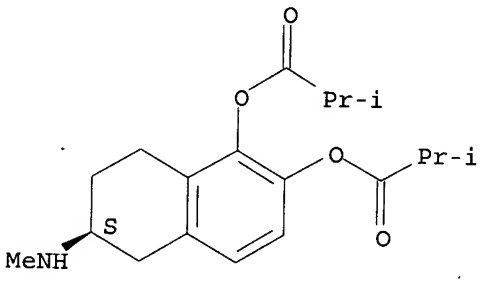


I

AB .gamma.-Cyclodextrin was used to perform chiral discrimination of (.+-.)-5,6-diisobutyroyl-2-methylaminotetralin-HCl (I) by 1H-NMR; the 95% enantiomeric excess of the (-)-isomer was detd. successfully.

L2 ANSWER 13 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 138531-49-4 REGISTRY
CN Propanoic acid, 2-methyl-, 5,6,7,8-tetrahydro-6-(methylamino)-1,2-naphthalenediyl ester, hydrochloride, (S)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN (-)-(S)-5,6-Diisobutyroyloxy-2-methylaminotetralin hydrochloride
FS STEREOSEARCH
DR 373380-15-5
MF C19 H27 N O4 . Cl H
SR CA
LC STN Files: CA, CAPLUS, CASREACT, DRUGPAT, DRUGUPDATES
CRN (146085-50-9)

Absolute stereochemistry. Rotation (-).



● HCl

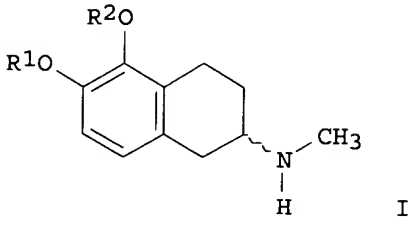
2 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1

AN 135:357780 CA
TI Optically active 2-aminotetralin derivatives, the processes for the preparation thereof, and the therapeutic use of pharmaceutical compositions containing them as antihypertensives, etc.
IN Amari, Gabriele; Del Canale, Maurizio; Razzetti, Roberta; Monici Preti, Pier Alessandro; Rondelli, Ivano
PA Chiesi Farmaceutici S.p.A., Italy
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001085668	A1	20011115	WO 2001-EP5212	20010508
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	IT 2000MI1053	A1	20011112	IT 2000-MI1053	20000512
	EP 1280759	A1	20030205	EP 2001-940415	20010508
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	NO 2002005393	A	20030113	NO 2002-5393	20021111

PRAI IT 2000-MI1053 20000512
WO 2001-EP5212 20010508
GI



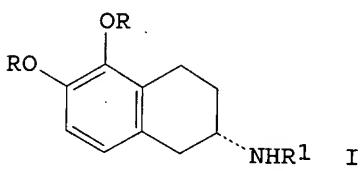
I

AB The invention concerns the use of the optically active forms of 5,6-dihydroxy-2-methylaminotetralin and their acyl esters, namely I [R1, R2 = H, C1-4 acyl], and their pharmaceutically acceptable salts, as medicaments. Also disclosed are a process for prepn. of I, and the use of I in pharmaceutical compns. Examples illustrate the prepn. of (+)- and (-)-I [R1 = R2 = isobutyroyl (II)] and the biol. activity of (+)- and (-)-I [R1 = R2 = H (III)]. For instance, (.+-.)-II.HCl was resolved using (-)-L- and (+)-D-dibenzoyltartaric acids to give (+)-(R)- and (-)-(S)-II.HCl with > 99% enantiomeric excess (ee) in both cases. Alternatively, 3-methoxycarbonylamino-5-(2,3-dimethoxyphenyl)-2,5-dihydrofuran-2-one underwent asym. hydrogenation using rhodium-(R,R)- or -(S,S)-EtDuPhos(COD)OTs complex as chiral catalysts, to give (+)-(S)- or (-)-(R)-2,3-(MeO)2C6H3CH2CH2CH(NHCO2Me)CO2H with 92% and 95% ee, resp. Cyclization of the acids to give tetralones, redn. of carbonyl, N-methylation, hydrolysis, O-demethylation, and esterification with isobutyroyl chloride in CF3CO2H, gave (+)-(R)- and (-)-(S)-II.HCl with approx. 95% ee in both cases. In several receptor assays, (-)-(S)-III showed 20 times the affinity for D2 dopaminergic receptors, and 10 times the affinity for .alpha.2 receptors, when compared to its enantiomer (+)-(R)-III, while showing similar activity at D1, .alpha.1, .beta.1, and .beta.2 receptors. This difference in activity was reflected in animal expts. using spontaneously hypertensive rats.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

REFERENCE 2

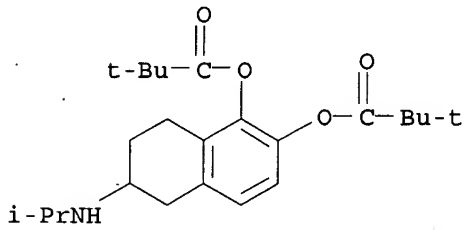
AN 116:59832 CA
TI Application of .gamma.-cyclodextrins to enantiomeric purity determination of 2-amino-tetralins by proton NMR spectroscopy
AU Redenti, E.; Bovis, G.; Fronza, G.; Ventura, P.
CS Chem. Biopharm. Dep., Chiesi Farm., Parma, 43100, Italy
SO Minutes Int. Symp. Cyclodextrins, 5th (1990), 669-71. Editor(s): Duchene, Dominique. Publisher: Ed. Sante, Paris, Fr.
CODEN: 57LSAJ
DT Conference
LA English
GI



I

AB A symposium on the chiral resoln. of (.+-.)-5,6-disubstituted-2-amino-tetralins, e.g. I (R = R1 = Me; R = COCHMe2, R1 = Me), using .gamma.-cyclodextrin. The enantiomeric excess of (-)-I was detd. successfully.

L2 ANSWER 14 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 90060-44-9 REGISTRY
CN Propanoic acid, 2,2-dimethyl-, 5,6,7,8-tetrahydro-6-[(1-methylethyl)amino]-1,2-naphthalenediyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H35 N O4
CI COM
LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

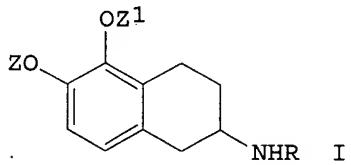
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1

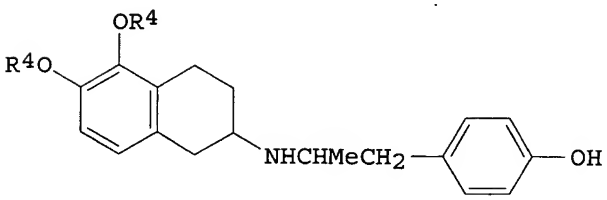
AN 100:191603 CA
TI 1,2,3,4-Tetrahydronaphthalene derivatives and compositions containing them
IN Chiesi, Paolo; Villani, Vlavio
PA Chiesi Farmaceutici S.p.A., Italy
SO Ger. Offen., 33 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3320936	A1	19831222	DE 1983-3320936	19830609
	DE 3320936	C2	19921119		
	GB 2123410	A1	19840201	GB 1983-15673	19830608
	GB 2123410	B2	19860828		
	FR 2528422	A1	19831216	FR 1983-9626	19830610
	FR 2528422	B1	19871030		
PRAI	IT 1982-21801		19820610		

GI



I

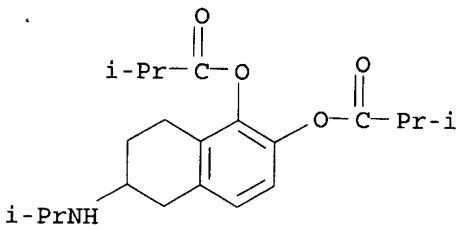


II

AB Tetrahydronaphthalenes I [R = H, C1-4 alkyl, C4-7 cycloalkyl, CR1R2(CH2)nPh; R1, R2 = H, C1-4 alkyl; n = 1, 2; the Ph (un)substituted by

1 or several halo, OH, MeO, OCH2O; Z, Z1 = H, C1-4 alkyl, C3-7 cycloalkyl, Z2R3; Z2 = CO, SO2; R3 = C1-15 alkyl, Ph (un)substituted by C1-4 alkyl] and their physiol. tolerable salts, having sympathomimetic activity and useful as uterus relaxants, vasoconstrictors, parkinsonism inhibitors (no data), and bronchodilators, were prepd. Condensing 5,6-dimethoxy-3,4-dihydro-2(1H)-naphthalenone with 4-HOC6H4CH2CH(NH2)Me.HBr in MeOH contg. K2CO3 and reducing the product in situ with NaBH3CN gave II (R4 = Me), isolated as the HCl salt. This diether was cleaved with HBr to give 82% II (R4 = H).HBr which had ID50 of 1.6 nmol/kg (guinea pigs) against histamine-induced bronchospasm.

L2 ANSWER 15 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 90060-43-8 REGISTRY
CN Propanoic acid, 2-methyl-, 5,6,7,8-tetrahydro-6-[(1-methylethyl)amino]-1,2-naphthalenediyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C21 H31 N O4
CI COM
LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

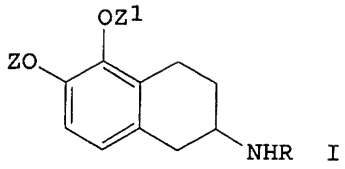
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1

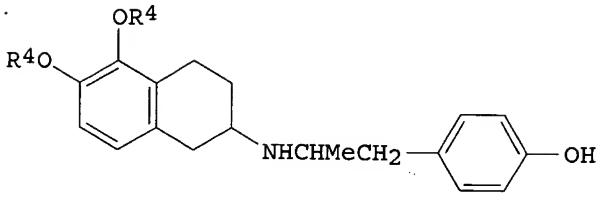
AN 100:191603 CA
TI 1,2,3,4-Tetrahydronaphthalene derivatives and compositions containing them
IN Chiesi, Paolo; Villani, Vlavio
PA Chiesi Farmaceutici S.p.A., Italy
SO Ger. Offen., 33 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3320936	A1	19831222	DE 1983-3320936	19830609
	DE 3320936	C2	19921119		
	GB 2123410	A1	19840201	GB 1983-15673	19830608
	GB 2123410	B2	19860828		
	FR 2528422	A1	19831216	FR 1983-9626	19830610
	FR 2528422	B1	19871030		
PRAI	IT 1982-21801		19820610		

GI



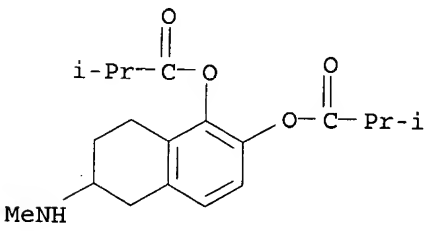
I



II

AB Tetrahydronaphthalenes I [R = H, C1-4 alkyl, C4-7 cycloalkyl, CR1R2(CH2)nPh; R1, R2 = H, C1-4 alkyl; n = 1, 2; the Ph (un)substituted by 1 or several halo, OH, MeO, OCH2O; Z, Z1 = H, C1-4 alkyl, C3-7 cycloalkyl, Z2R3; Z2 = CO, SO2; R3 = C1-15 alkyl, Ph (un)substituted by C1-4 alkyl] and their physiol. tolerable salts, having sympathomimetic activity and useful as uterus relaxants, vasoconstrictors, parkinsonism inhibitors (no data), and bronchodilators, were prepd. Condensing 5,6-dimethoxy-3,4-dihydro-2(1H)-naphthalenone with 4-HOC6H4CH2CH(NH2)Me.HBr in MeOH contg. K2CO3 and reducing the product in situ with NaBH3CN gave II (R4 = Me), isolated as the HCl salt. This diether was cleaved with HBr to give 82% II (R4 = H).HBr which had ID50 of 1.6 nmol/kg (guinea pigs) against histamine-induced bronchospasm.

L2 ANSWER 16 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 90060-42-7 REGISTRY
CN Propanoic acid, 2-methyl-, 5,6,7,8-tetrahydro-6-(methylamino)-1,2-naphthalenediyl ester (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Nolomirole
FS 3D CONCORD
DR 146085-48-5
MF C19 H27 N O4
CI COM
LC STN Files: ADISINSIGHT, CA, CAPLUS, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, SYNTHLINE, USPATFULL
Other Sources: WHO



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

7 REFERENCES IN FILE CA (1957 TO DATE)
7 REFERENCES IN FILE CAPLUS (1957 TO DATE)

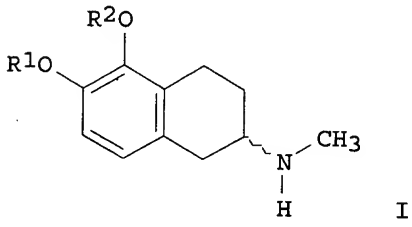
REFERENCE 1

AN 135:357780 CA
TI Optically active 2-aminotetralin derivatives, the processes for the preparation thereof, and the therapeutic use of pharmaceutical compositions containing them as antihypertensives, etc.
IN Amari, Gabriele; Del Canale, Maurizio; Razzetti, Roberta; Monici Preti, Pier Alessandro; Rondelli, Ivano

PA Chiesi Farmaceutici S.p.A., Italy
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001085668	A1	20011115	WO 2001-EP5212	20010508
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	IT 2000MI1053	A1	20011112	IT 2000-MI1053	20000512
	EP 1280759	A1	20030205	EP 2001-940415	20010508
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	NO 2002005393	A	20030113	NO 2002-5393	20021111
PRAI	IT 2000-MI1053	20000512			
	WO 2001-EP5212	20010508			

GI



I

AB The invention concerns the use of the optically active forms of 5,6-dihydroxy-2-methylaminotetralin and their acyl esters, namely I [R1, R2 = H, C1-4 acyl], and their pharmaceutically acceptable salts, as medicaments. Also disclosed are a process for prepn. of I, and the use of I in pharmaceutical compns. Examples illustrate the prepn. of (+)- and (-)-I [R1 = R2 = isobutyroyl (II)] and the biol. activity of (+)- and (-)-I [R1 = R2 = H (III)]. For instance, (.+-.)-II.HCl was resolved using (-)-L- and (+)-D-dibenzoyltartaric acids to give (+)-(R)- and (-)-(S)-II.HCl with > 99% enantiomeric excess (ee) in both cases. Alternatively, 3-methoxycarbonylamino-5-(2,3-dimethoxyphenyl)-2,5-dihydrofuran-2-one underwent asym. hydrogenation using rhodium-(R,R)- or -(S,S)-EtDuPhos(COD)OTs complex as chiral catalysts, to give (+)-(S)- or (-)-(R)-2,3-(MeO)2C6H3CH2CH2CH(NHCO2Me)CO2H with 92% and 95% ee, resp. Cyclization of the acids to give tetralones, redn. of carbonyl, N-methylation, hydrolysis, O-demethylation, and esterification with isobutyroyl chloride in CF3CO2H, gave (+)-(R)- and (-)-(S)-II.HCl with approx. 95% ee in both cases. In several receptor assays, (-)-(S)-III showed 20 times the affinity for D2 dopaminergic receptors, and 10 times the affinity for .alpha.2 receptors, when compared to its enantiomer (+)-(R)-III, while showing similar activity at D1, .alpha.1, .beta.1, and .beta.2 receptors. This difference in activity was reflected in animal expts. using spontaneously hypertensive rats.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

REFERENCE 2

AN 134:125975 CA
TI 2-Aminotetralin derivatives for the therapy of glaucoma
IN Bongrani, Stefano; Razzetti, Roberta; Chiesi, Paolo

PA Chiesi Farmaceutici S.P.A., Italy
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001008667	A2	20010208	WO 2000-EP7184	20000726
	WO 2001008667	A3	20010607		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	IT 99MI1713	A1	20010130	IT 1999-MI1713	19990730
	EP 1200079	A2	20020502	EP 2000-956296	20000726
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	JP 2003505499	T2	20030212	JP 2001-513397	20000726
	NO 2002000475	A	20020313	NO 2002-475	20020129
PRAI	IT 1999-MI1713	19990730			
	WO 2000-EP7184	20000726			

AB Disclosed is the use of racemic or optically active compds. of 5,6-diisobutyroyloxy-2-methylaminotetralin, 5,6-diisobutyroyloxy-2-aminotetralin, and salts thereof for the prepn. of pharmaceutical compns. for the therapy of ophthalmic disorders. Intraocular pressure-lowering activities of CHF 1035 were tested with rabbits.

REFERENCE 3

AN 126:220252 CA
TI New method for the resolution of the enantiomers of 5,6-dihydroxy-2-methyl-aminotetralin by selective derivatization and HPLC. [Erratum to document cited in CA125:316086]
AU Rondelli, Ivano; Corsaletti, Roberto; Redenti, Enrico; Acerbi, Daniela; Delcanale, Maurizio; Amari, Gabriele; Ventura, Paolo
CS Chemical Biopharmaceutical Direction, Parma, Italy
SO Chirality (1997), 9(1), 89
CODEN: CHRLEP; ISSN: 0899-0042
PB Wiley-Liss
DT Journal
LA English
AB The errors were not reflected in the abstr. or the index entries.

REFERENCE 4

AN 125:317359 CA
TI Aminotetralin derivative for the therapy of cardiovascular diseases
IN Chiesi, Paolo; Bongrani, Stefano; Razetti, Roberta; Civelli, Maurizio; Umile, Alberto
PA Chiesi Farmaceutici S.P.A., Italy
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9629065	A2	19960926	WO 1996-EP1060	19960313
	WO 9629065	A3	19961128		
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN

CA 2215671	AA	19960926	CA 1996-2215671	19960313
AU 9651072	A1	19961008	AU 1996-51072	19960313
AU 702656	B2	19990225		
EP 814791	A1	19980107	EP 1996-907446	19960313
EP 814791	B1	20020612		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

CN 1181699	A	19980513	CN 1996-193312	19960313
BR 9607996	A	19980623	BR 1996-7996	19960313
JP 11502211	T2	19990223	JP 1996-528045	19960313
NZ 303993	A	20001222	NZ 1996-303993	19960313
CZ 288488	B6	20010613	CZ 1997-2866	19960313
AT 218856	E	20020615	AT 1996-907446	19960313
EP 1216702	A2	20020626	EP 2002-1772	19960313
EP 1216702	A3	20020904		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PL 183347	B1	20020628	PL 1996-322284	19960313
ES 2177769	T3	20021216	ES 1996-907446	19960313
EE 4040	B1	20030616	EE 1997-231	19960313
ZA 9602073	A	19960925	ZA 1996-2073	19960314
IL 117518	A1	20010520	IL 1996-117518	19960317
LV 11882	B	19980320	LV 1997-166	19970915
LT 4355	B	19980625	LT 1997-147	19970915
NO 9704267	A	19971107	NO 1997-4267	19970916
US 6013678	A	20000111	US 1997-913363	19971014
US 6103760	A	20000815	US 1999-328434	19990609
WO 2000076544	A1	20001221	WO 2000-EP5231	20000607

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1183046	A1	20020306	EP 2000-935184	20000607

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

BR 2000012121	A	20020514	BR 2000-12121	20000607
JP 2003501483	T2	20030114	JP 2001-502876	20000607
EE 200100663	A	20030415	EE 2001-663	20000607
NO 2001006000	A	20020211	NO 2001-6000	20011207
US 6576671	B1	20030610	US 2002-9352	20020219

PRAI	IT 1995-MI532	19950317
	EP 1996-907446	19960313
	WO 1996-EP1060	19960313
	US 1999-328434	19990609
	WO 2000-EP5231	20000607

AB The use of 5,6-diisobutyroyloxy-2-methylaminotetralin (I) at 2.5-20 mg/day for the therapy of cardiac disorders, particularly of congestive heart failure is described. The pharmacol. effects of I (5, 10 or 15 mg) on the hemodynamic parameters and the neurohumoral pattern was carried out in 18 patients. I induced a significant improvement in hemodynamic parameters and systemic vasodilation without inducing any reflected increase in catecholamine plasma levels.

REFERENCE 5

AN 125:316086 CA

TI New method for the resolution of the enantiomers of 5,6-dihydroxy-2-methyl-aminotetralin by selective derivatization and HPLC analysis: application to biological fluids

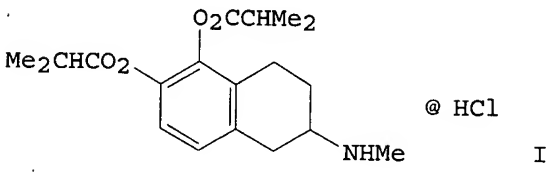
AU Rondelli, Ivano; Corsaletti, Roberto; Redenti, Enrico; Acerbi, Daniela; Delcanale, Maurizio; Amari, Gabriele; Ventura, Paolo

CS Chemical Biopharmaceutical Direction, Chiesi Farmaceutici S.p.A., Parma,

Italy
SO Chirality (1996), 8(5), 381-389
CODEN: CHRLEP; ISSN: 0899-0042
PB Wiley-Liss
DT Journal
LA English
AB A new chiral derivatization procedure for the HPLC resoln. of chiral catecholamines and structurally related compds. is described. The homochiral reagent, (+)-(R)-1-phenylethyl isocyanate (RPEIC), was added to sep. and quantitate the enantiomers of rac-5,6-dihydroxy-2-methyl-aminotetralin, the main metabolite of rac-5,6-diisobutyryl-2-methyl-aminotetralin, a potent dopamine agonist, by reversed-phase HPLC anal. To avoid catecholamine degrdn. in the basic reaction medium and to obtain the selective and quant. derivatization of the amino group of the compd., the reversible complex formation between diphenylborinic acid (DPBA) and the catechol group, in alk. medium, was performed before homochiral isocyanate addn. The RPEIC derivatization was completed in 30 min and then the DPBA complex was dissocd. by adding dil. acid. The structure of intermediates and urea derivs. was confirmed by mass spectrometry. The use of an electrochem. detector, operating in redox mode, allowed HPLC quantitation of enantiomers at the nanogram level in plasma and urine. The derivatization procedure is also suitable for other catecholamine-related compds.

REFERENCE 6

AN 118:154695 CA
TI Application of .gamma.-cyclodextrin to enantiomeric purity determination of a new 2-aminotetralin derivative by proton NMR spectroscopy
AU Redenti, Enrico; Fronza, Giovanni; Bovis, Giovanni; Ventura, Paolo
CS Chem. Biopharm. Dep., Chiesi Farm. S.p.A., Parma, I-43100, Italy
SO Chirality (1992), 4(6), 404-5
CODEN: CHRLEP; ISSN: 0899-0042
DT Journal
LA English
GI



I

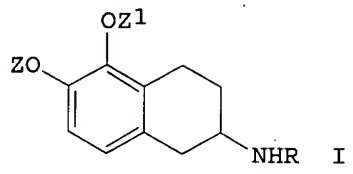
AB .gamma.-Cyclodextrin was used to perform chiral discrimination of (.+-.)-5,6-diisobutyroyl-2-methylaminotetralin-HCl (I) by 1H-NMR; the 95% enantiomeric excess of the (-)-isomer was detd. successfully.

REFERENCE 7

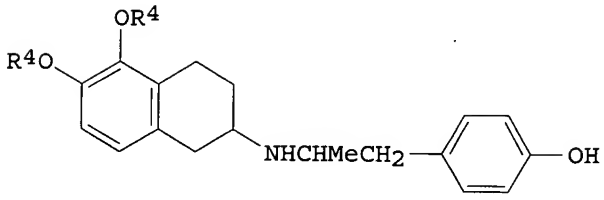
AN 100:191603 CA
TI 1,2,3,4-Tetrahydronaphthalene derivatives and compositions containing them
IN Chiesi, Paolo; Villani, Vlavio
PA Chiesi Farmaceutici S.p.A., Italy
SO Ger. Offen., 33 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3320936	A1	19831222	DE 1983-3320936	19830609
	DE 3320936	C2	19921119		
	GB 2123410	A1	19840201	GB 1983-15673	19830608
	GB 2123410	B2	19860828		
	FR 2528422	A1	19831216	FR 1983-9626	19830610

FR 2528422 B1 19871030
PRAI IT 1982-21801 19820610
GI



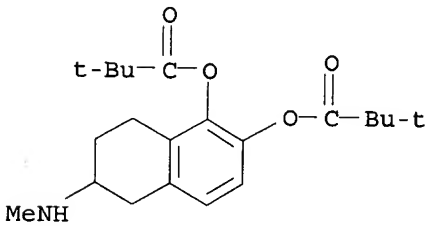
I



II

AB Tetrahydronaphthalenes I [R = H, C1-4 alkyl, C4-7 cycloalkyl, CR1R2(CH2)nPh; R1, R2 = H, C1-4 alkyl; n = 1, 2; the Ph (un)substituted by 1 or several halo, OH, MeO, OCH2O; Z, Z1 = H, C1-4 alkyl, C3-7 cycloalkyl, Z2R3; Z2 = CO, SO2; R3 = C1-15 alkyl, Ph (un)substituted by C1-4 alkyl] and their physiol. tolerable salts, having sympathomimetic activity and useful as uterus relaxants, vasoconstrictors, parkinsonism inhibitors (no data), and bronchodilators, were prepd. Condensing 5,6-dimethoxy-3,4-dihydro-2(1H)-naphthalenone with 4-HOC6H4CH2CH(NH2)Me.HBr in MeOH contg. K2CO3 and reducing the product in situ with NaBH3CN gave II (R4 = Me), isolated as the HCl salt. This diether was cleaved with HBr to give 82% II (R4 = H).HBr which had ID50 of 1.6 nmol/kg (guinea pigs) against histamine-induced bronchospasm.

L2 ANSWER 17 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 90060-41-6 REGISTRY
CN Propanoic acid, 2,2-dimethyl-, 5,6,7,8-tetrahydro-6-(methylamino)-1,2-naphthalenediyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C21 H31 N O4
CI COM
LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

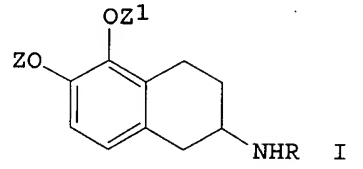
REFERENCE 1

AN 100:191603 CA
TI 1,2,3,4-Tetrahydronaphthalene derivatives and compositions containing them
IN Chiesi, Paolo; Villani, Vlavio
PA Chiesi Farmaceutici S.p.A., Italy

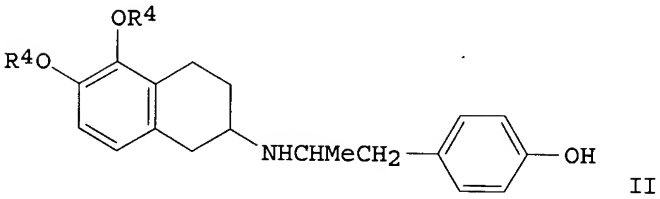
SO Ger. Offen., 33 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3320936	A1	19831222	DE 1983-3320936	19830609
	DE 3320936	C2	19921119		
	GB 2123410	A1	19840201	GB 1983-15673	19830608
	GB 2123410	B2	19860828		
	FR 2528422	A1	19831216	FR 1983-9626	19830610
	FR 2528422	B1	19871030		
PRAI	IT 1982-21801	19820610			

GI



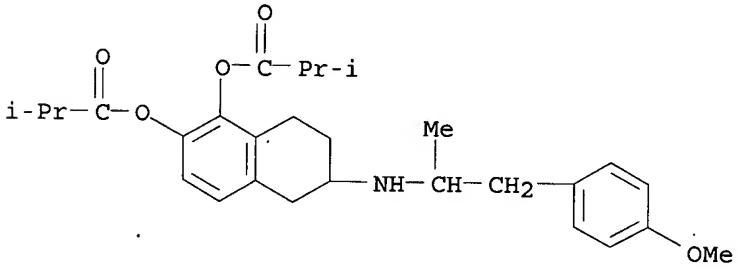
I



II

AB Tetrahydronaphthalenes I [R = H, C1-4 alkyl, C4-7 cycloalkyl, CR1R2(CH2)nPh; R1, R2 = H, C1-4 alkyl; n = 1, 2; the Ph (un)substituted by 1 or several halo, OH, MeO, OCH2O; Z, Z1 = H, C1-4 alkyl, C3-7 cycloalkyl, Z2R3; Z2 = CO, SO2; R3 = C1-15 alkyl, Ph (un)substituted by C1-4 alkyl] and their physiol. tolerable salts, having sympathomimetic activity and useful as uterus relaxants, vasoconstrictors, parkinsonism inhibitors (no data), and bronchodilators, were prepd. Condensing 5,6-dimethoxy-3,4-dihydro-2(1H)-naphthalenone with 4-HOC6H4CH2CH(NH2)Me.HBr in MeOH contg. K2CO3 and reducing the product in situ with NaBH3CN gave II (R4 = Me), isolated as the HCl salt. This diether was cleaved with HBr to give 82% II (R4 = H).HBr which had ID50 of 1.6 nmol/kg (guinea pigs) against histamine-induced bronchospasm.

L2 ANSWER 18 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 90060-36-9 REGISTRY
CN Propanoic acid, 2-methyl-, 5,6,7,8-tetrahydro-6-[[2-(4-methoxyphenyl)-1-methylethyl]amino]-1,2-naphthalenediyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C28 H37 N O5
CI COM
LC STN Files: CA, CAPLUS, CASREACT



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

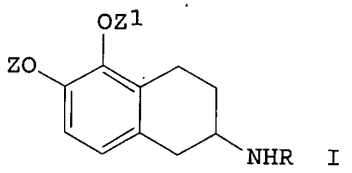
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1

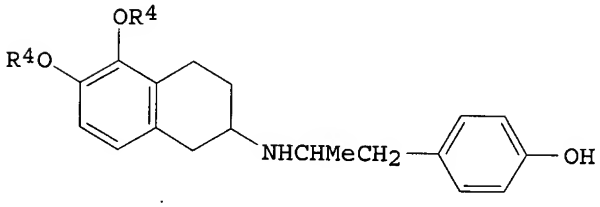
AN 100:191603 CA
TI 1,2,3,4-Tetrahydronaphthalene derivatives and compositions containing them
IN Chiesi, Paolo; Villani, Vlavio
PA Chiesi Farmaceutici S.p.A., Italy
SO Ger. Offen., 33 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3320936	A1	19831222	DE 1983-3320936	19830609
	DE 3320936	C2	19921119		
	GB 2123410	A1	19840201	GB 1983-15673	19830608
	GB 2123410	B2	19860828		
	FR 2528422	A1	19831216	FR 1983-9626	19830610
	FR 2528422	B1	19871030		
PRAI	IT 1982-21801		19820610		

GI



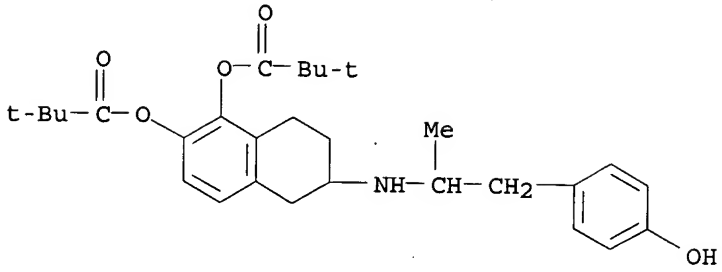
I



II

AB Tetrahydronaphthalenes I [R = H, C1-4 alkyl, C4-7 cycloalkyl, CR1R2(CH2)nPh; R1, R2 = H, C1-4 alkyl; n = 1, 2; the Ph (un)substituted by 1 or several halo, OH, MeO, OCH2O; Z, Z1 = H, C1-4 alkyl, C3-7 cycloalkyl, Z2R3; Z2 = CO, SO2; R3 = C1-15 alkyl, Ph (un)substituted by C1-4 alkyl] and their physiol. tolerable salts, having sympathomimetic activity and useful as uterus relaxants, vasoconstrictors, parkinsonism inhibitors (no data), and bronchodilators, were prepd. Condensing 5,6-dimethoxy-3,4-dihydro-2(1H)-naphthalenone with 4-HOC6H4CH2CH(NH2)Me.HBr in MeOH contg. K2CO3 and reducing the product in situ with NaBH3CN gave II (R4 = Me), isolated as the HCl salt. This diether was cleaved with HBr to give 82% II (R4 = H).HBr which had ID50 of 1.6 nmol/kg (guinea pigs) against histamine-induced bronchospasm.

L2 ANSWER 19 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 90060-35-8 REGISTRY
CN Propanoic acid, 2,2-dimethyl-, 5,6,7,8-tetrahydro-6-[[2-(4-hydroxyphenyl)-1-methylethyl]amino]-1,2-naphthalenediyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C29 H39 N O5
LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

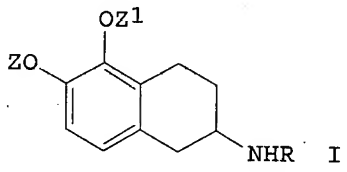
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1

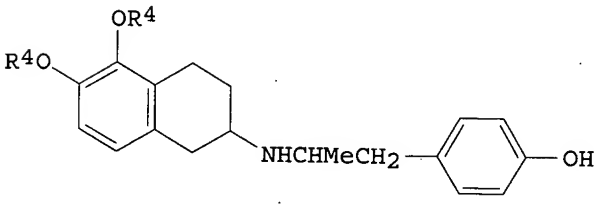
AN 100:191603 CA
TI 1,2,3,4-Tetrahydronaphthalene derivatives and compositions containing them
IN Chiesi, Paolo; Villani, Vlavio
PA Chiesi Farmaceutici S.p.A., Italy
SO Ger. Offen., 33 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3320936	A1	19831222	DE 1983-3320936	19830609
	DE 3320936	C2	19921119		
	GB 2123410	A1	19840201	GB 1983-15673	19830608
	GB 2123410	B2	19860828		
	FR 2528422	A1	19831216	FR 1983-9626	19830610
	FR 2528422	B1	19871030		
PRAI	IT 1982-21801		19820610		

GI



I

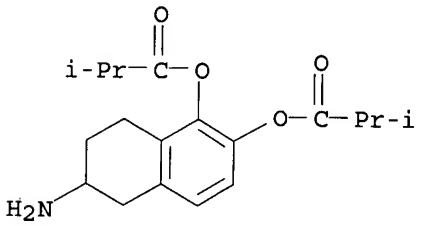


II

AB Tetrahydronaphthalenes I [R = H, C1-4 alkyl, C4-7 cycloalkyl, CR1R2(CH2)nPh; R1, R2 = H, C1-4 alkyl; n = 1, 2; the Ph (un)substituted by 1 or several halo, OH, MeO, OCH2O; Z, Z1 = H, C1-4 alkyl, C3-7 cycloalkyl, Z2R3; Z2 = CO, SO2; R3 = C1-15 alkyl, Ph (un)substituted by C1-4 alkyl] and their physiol. tolerable salts, having sympathomimetic activity and useful as uterus relaxants, vasoconstrictors, parkinsonism inhibitors (no data), and bronchodilators, were prepd. Condensing 5,6-dimethoxy-3,4-dihydro-2(1H)-naphthalenone with 4-HOC6H4CH2CH(NH2)Me.HBr in MeOH contg.

K2CO3 and reducing the product in situ with NaBH3CN gave II (R4 = Me), isolated as the HCl salt. This diether was cleaved with HBr to give 82% II (R4 = H).HBr which had ID50 of 1.6 nmol/kg (guinea pigs) against histamine-induced bronchospasm.

L2 ANSWER 20 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 90060-34-7 REGISTRY
CN Propanoic acid, 2-methyl-, 6-amino-5,6,7,8-tetrahydro-1,2-naphthalenediyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C18 H25 N O4
CI COM
LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1

AN 134:125975 CA
TI 2-Aminotetralin derivatives for the therapy of glaucoma
IN Bongrani, Stefano; Razzetti, Roberta; Chiesi, Paolo
PA Chiesi Farmaceutici S.P.A., Italy
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001008667	A2	20010208	WO 2000-EP7184	20000726
	WO 2001008667	A3	20010607		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	IT 99MI1713	A1	20010130	IT 1999-MI1713	19990730
	EP 1200079	A2	20020502	EP 2000-956296	20000726
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	JP 2003505499	T2	20030212	JP 2001-513397	20000726
	NO 2002000475	A	20020313	NO 2002-475	20020129
PRAI	IT 1999-MI1713	19990730			
	WO 2000-EP7184	20000726			

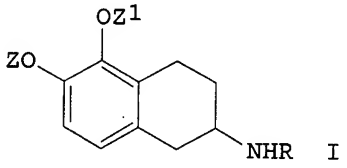
AB Disclosed is the use of racemic or optically active compds. of 5,6-diisobutyroyloxy-2-methylaminotetralin, 5,6-diisobutyroyloxy-2-aminotetralin, and salts thereof for the prepn. of pharmaceutical compns. for the therapy of ophthalmic disorders. Intraocular pressure-lowering activities of CHF 1035 were tested with rabbits.

REFERENCE 2

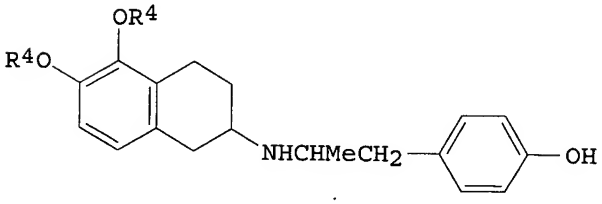
AN 100:191603 CA
TI 1,2,3,4-Tetrahydronaphthalene derivatives and compositions containing them
IN Chiesi, Paolo; Villani, Vlavio
PA Chiesi Farmaceutici S.p.A., Italy
SO Ger. Offen., 33 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3320936	A1	19831222	DE 1983-3320936	19830609
	DE 3320936	C2	19921119		
	GB 2123410	A1	19840201	GB 1983-15673	19830608
	GB 2123410	B2	19860828		
	FR 2528422	A1	19831216	FR 1983-9626	19830610
	FR 2528422	B1	19871030		
PRAI	IT 1982-21801		19820610		

GI



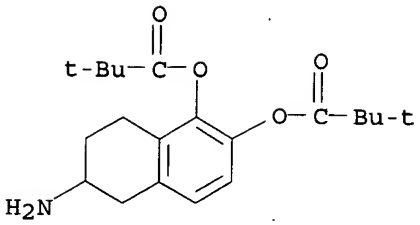
I



II

AB Tetrahydronaphthalenes I [R = H, C1-4 alkyl, C4-7 cycloalkyl, CR1R2(CH2)nPh; R1, R2 = H, C1-4 alkyl; n = 1, 2; the Ph (un)substituted by 1 or several halo, OH, MeO, OCH2O; Z, Z1 = H, C1-4 alkyl, C3-7 cycloalkyl, Z2R3; Z2 = CO, SO2; R3 = C1-15 alkyl, Ph (un)substituted by C1-4 alkyl] and their physiol. tolerable salts, having sympathomimetic activity and useful as uterus relaxants, vasoconstrictors, parkinsonism inhibitors (no data), and bronchodilators, were prepd. Condensing 5,6-dimethoxy-3,4-dihydro-2(1H)-naphthalenone with 4-HOC6H4CH2CH(NH2)Me.HBr in MeOH contg. K2CO3 and reducing the product in situ with NaBH3CN gave II (R4 = Me), isolated as the HCl salt. This diether was cleaved with HBr to give 82% II (R4 = H).HBr which had ID50 of 1.6 nmol/kg (guinea pigs) against histamine-induced bronchospasm.

L2 ANSWER 21 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 90060-33-6 REGISTRY
CN Propanoic acid, 2,2-dimethyl-, 6-amino-5,6,7,8-tetrahydro-1,2-naphthalenediyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C20 H29 N O4
CI COM
LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

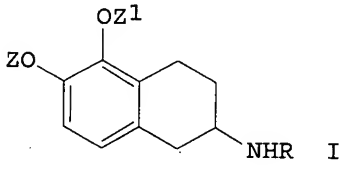
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1

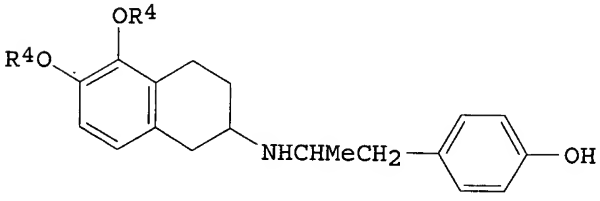
AN 100:191603 CA
TI 1,2,3,4-Tetrahydronaphthalene derivatives and compositions containing them
IN Chiesi, Paolo; Villani, Vlavio
PA Chiesi Farmaceutici S.p.A., Italy
SO Ger. Offen., 33 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3320936	A1	19831222	DE 1983-3320936	19830609
	DE 3320936	C2	19921119		
	GB 2123410	A1	19840201	GB 1983-15673	19830608
	GB 2123410	B2	19860828		
	FR 2528422	A1	19831216	FR 1983-9626	19830610
	FR 2528422	B1	19871030		
PRAI	IT 1982-21801		19820610		

GI



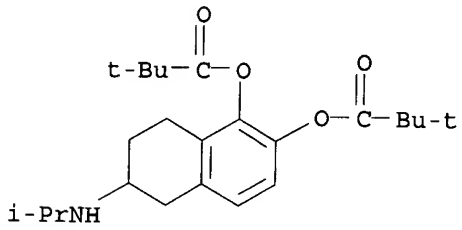
I



II

AB Tetrahydronaphthalenes I [R = H, C1-4 alkyl, C4-7 cycloalkyl, CR1R2(CH2)nPh; R1, R2 = H, C1-4 alkyl; n = 1, 2; the Ph (un)substituted by 1 or several halo, OH, MeO, OCH2O; Z, Z1 = H, C1-4 alkyl, C3-7 cycloalkyl, Z2R3; Z2 = CO, SO2; R3 = C1-15 alkyl, Ph (un)substituted by C1-4 alkyl] and their physiol. tolerable salts, having sympathomimetic activity and useful as uterus relaxants, vasoconstrictors, parkinsonism inhibitors (no data), and bronchodilators, were prepd. Condensing 5,6-dimethoxy-3,4-dihydro-2(1H)-naphthalenone with 4-HOC6H4CH2CH(NH2)Me.HBr in MeOH contg. K2CO3 and reducing the product in situ with NaBH3CN gave II (R4 = Me), isolated as the HCl salt. This diether was cleaved with HBr to give 82% II (R4 = H).HBr which had ID50 of 1.6 nmol/kg (guinea pigs) against histamine-induced bronchospasm.

L2 ANSWER 22 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 90060-23-4 REGISTRY
CN Propanoic acid, 2,2-dimethyl-, 5,6,7,8-tetrahydro-6-[(1-methylethyl)amino]-1,2-naphthalenediyl ester, hydrobromide (9CI) (CA INDEX NAME)
MF C23 H35 N O4 . Br H
LC STN Files: CA, CAPLUS
CRN (90060-44-9)



● HBr

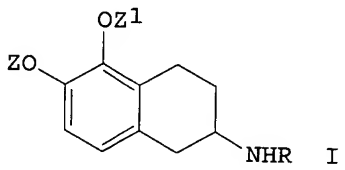
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1

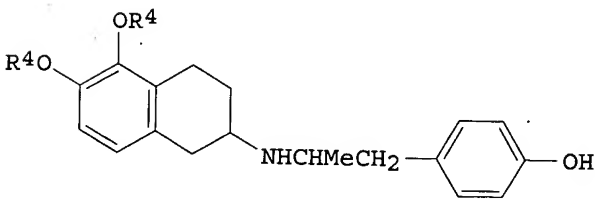
AN 100:191603 CA
TI 1,2,3,4-Tetrahydronaphthalene derivatives and compositions containing them
IN Chiesi, Paolo; Villani, Vlavio
PA Chiesi Farmaceutici S.p.A., Italy
SO Ger. Offen., 33 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3320936	A1	19831222	DE 1983-3320936	19830609
	DE 3320936	C2	19921119		
	GB 2123410	A1	19840201	GB 1983-15673	19830608
	GB 2123410	B2	19860828		
	FR 2528422	A1	19831216	FR 1983-9626	19830610
	FR 2528422	B1	19871030		
PRAI	IT 1982-21801		19820610		

GI



I

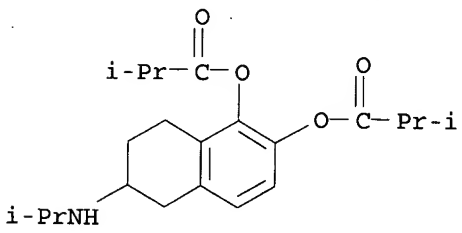


II

AB Tetrahydronaphthalenes I [R = H, C1-4 alkyl, C4-7 cycloalkyl,

CR1R2(CH2)nPh; R1, R2 = H, C1-4 alkyl; n = 1, 2; the Ph (un)substituted by 1 or several halo, OH, MeO, OCH2O; Z, Z1 = H, C1-4 alkyl, C3-7 cycloalkyl, Z2R3; Z2 = CO, SO2; R3 = C1-15 alkyl, Ph (un)substituted by C1-4 alkyl] and their physiol. tolerable salts, having sympathomimetic activity and useful as uterus relaxants, vasoconstrictors, parkinsonism inhibitors (no data), and bronchodilators, were prepd. Condensing 5,6-dimethoxy-3,4-dihydro-2(1H)-naphthalenone with 4-HOC6H4CH2CH(NH2)Me.HBr in MeOH contg. K2CO3 and reducing the product in situ with NaBH3CN gave II (R4 = Me), isolated as the HCl salt. This diether was cleaved with HBr to give 82% II (R4 = H).HBr which had ID50 of 1.6 nmol/kg (guinea pigs) against histamine-induced bronchospasm.

L2 ANSWER 23 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 90060-22-3 REGISTRY
CN Propanoic acid, 2-methyl-, 5,6,7,8-tetrahydro-6-[(1-methylethyl)amino]-1,2-naphthalenediyl ester, hydrobromide (9CI) (CA INDEX NAME)
MF C21 H31 N O4 . Br H
LC STN Files: CA, CAPLUS
CRN (90060-43-8)



● HBr

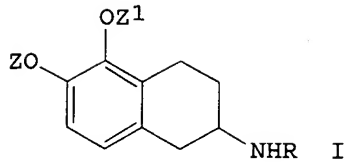
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1

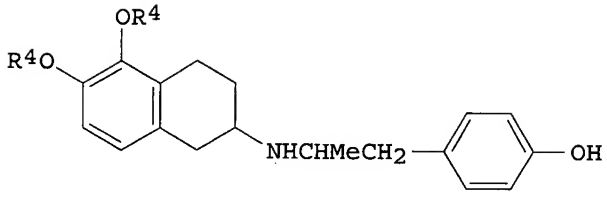
AN 100:191603 CA
TI 1,2,3,4-Tetrahydronaphthalene derivatives and compositions containing them
IN Chiesi, Paolo; Villani, Vlavio
PA Chiesi Farmaceutici S.p.A., Italy
SO Ger. Offen., 33 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3320936	A1	19831222	DE 1983-3320936	19830609
	DE 3320936	C2	19921119		
	GB 2123410	A1	19840201	GB 1983-15673	19830608
	GB 2123410	B2	19860828		
	FR 2528422	A1	19831216	FR 1983-9626	19830610
	FR 2528422	B1	19871030		
PRAI	IT 1982-21801		19820610		

GI



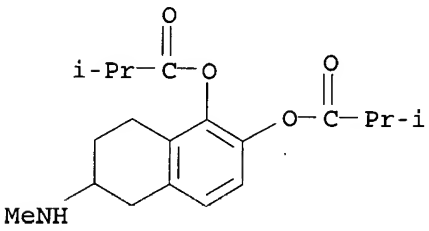
I



II

AB Tetrahydronaphthalenes I [R = H, C1-4 alkyl, C4-7 cycloalkyl, CR1R2(CH2)nPh; R1, R2 = H, C1-4 alkyl; n = 1, 2; the Ph (un)substituted by 1 or several halo, OH, MeO, OCH2O; Z, Z1 = H, C1-4 alkyl, C3-7 cycloalkyl, Z2R3; Z2 = CO, SO2; R3 = C1-15 alkyl, Ph (un)substituted by C1-4 alkyl] and their physiol. tolerable salts, having sympathomimetic activity and useful as uterus relaxants, vasoconstrictors, parkinsonism inhibitors (no data), and bronchodilators, were prepd. Condensing 5,6-dimethoxy-3,4-dihydro-2(1H)-naphthalenone with 4-HOC6H4CH2CH(NH2)Me.HBr in MeOH contg. K2CO3 and reducing the product in situ with NaBH3CN gave II (R4 = Me), isolated as the HCl salt. This diether was cleaved with HBr to give 82% II (R4 = H).HBr which had ID50 of 1.6 nmol/kg (guinea pigs) against histamine-induced bronchospasm.

L2 ANSWER 24 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 90060-21-2 REGISTRY
CN Propanoic acid, 2-methyl-, 5,6,7,8-tetrahydro-6-(methylamino)-1,2-naphthalenediyl ester, hydrobromide (9CI) (CA INDEX NAME)
MF C19 H27 N O4 . Br H
LC STN Files: CA, CAPLUS, DRUGPAT, DRUGUPDATES
CRN (90060-42-7)



● HBr

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

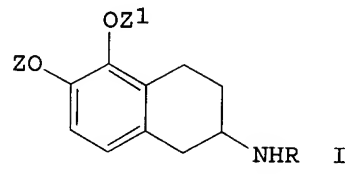
REFERENCE 1

AN 100:191603 CA
TI 1,2,3,4-Tetrahydronaphthalene derivatives and compositions containing them
IN Chiesi, Paolo; Villani, Vlavio
PA Chiesi Farmaceutici S.p.A., Italy
SO Ger. Offen., 33 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

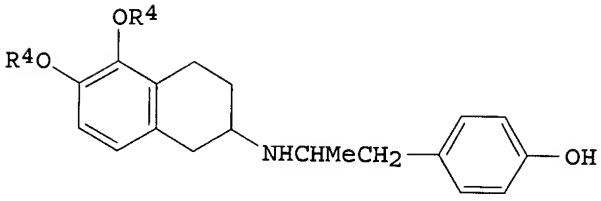
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	DE 3320936	A1	19831222	DE 1983-3320936	19830609
	DE 3320936	C2	19921119		
	GB 2123410	A1	19840201	GB 1983-15673	19830608
	GB 2123410	B2	19860828		
	FR 2528422	A1	19831216	FR 1983-9626	19830610
	FR 2528422	B1	19871030		
PRAI	IT 1982-21801	19820610			

GI



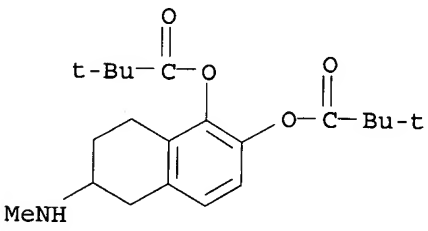
I



II

AB Tetrahydronaphthalenes I [R = H; C1-4 alkyl, C4-7 cycloalkyl, CR1R2(CH2)nPh; R1, R2 = H, C1-4 alkyl; n = 1, 2; the Ph (un)substituted by 1 or several halo, OH, MeO, OCH2O; Z, Z1 = H, C1-4 alkyl, C3-7 cycloalkyl, Z2R3; Z2 = CO, SO2; R3 = C1-15 alkyl, Ph (un)substituted by C1-4 alkyl] and their physiol. tolerable salts, having sympathomimetic activity and useful as uterus relaxants, vasoconstrictors, parkinsonism inhibitors (no data), and bronchodilators, were prepd. Condensing 5,6-dimethoxy-3,4-dihydro-2(1H)-naphthalenone with 4-HOC6H4CH2CH(NH2)Me.HBr in MeOH contg. K2CO3 and reducing the product in situ with NaBH3CN gave II (R4 = Me), isolated as the HCl salt. This diether was cleaved with HBr to give 82% II (R4 = H).HBr which had ID50 of 1.6 nmol/kg (guinea pigs) against histamine-induced bronchospasm.

L2 ANSWER 25 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 90060-19-8 REGISTRY
CN Propanoic acid, 2,2-dimethyl-, 5,6,7,8-tetrahydro-6-(methylamino)-1,2-naphthalenediyl ester, hydrobromide (9CI) (CA INDEX NAME)
MF C21 H31 N O4 . Br H
LC STN Files: CA, CAPLUS
CRN (90060-41-6)



HBr

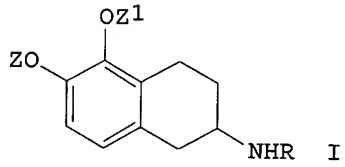
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1

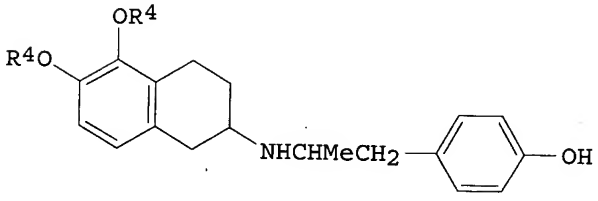
AN 100:191603 CA
TI 1,2,3,4-Tetrahydronaphthalene derivatives and compositions containing them
IN Chiesi, Paolo; Villani, Vlavio
PA Chiesi Farmaceutici S.p.A., Italy
SO Ger. Offen., 33 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3320936	A1	19831222	DE 1983-3320936	19830609
	DE 3320936	C2	19921119		
	GB 2123410	A1	19840201	GB 1983-15673	19830608
	GB 2123410	B2	19860828		
	FR 2528422	A1	19831216	FR 1983-9626	19830610
	FR 2528422	B1	19871030		
PRAI	IT 1982-21801		19820610		

GI



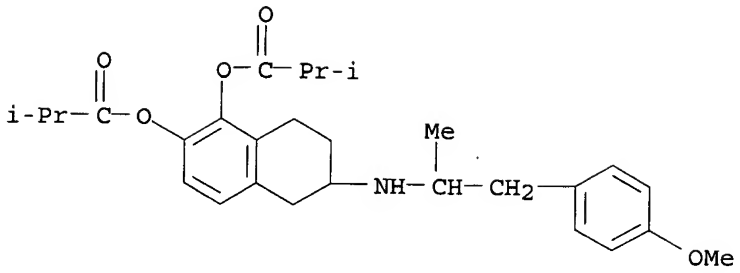
I



II

AB Tetrahydronaphthalenes I [R = H, C1-4 alkyl, C4-7 cycloalkyl, CR1R2(CH2)nPh; R1, R2 = H, C1-4 alkyl; n = 1, 2; the Ph (un)substituted by 1 or several halo, OH, MeO, OCH2O; Z, Z1 = H, C1-4 alkyl, C3-7 cycloalkyl, Z2R3; Z2 = CO, SO2; R3 = C1-15 alkyl, Ph (un)substituted by C1-4 alkyl] and their physiol. tolerable salts, having sympathomimetic activity and useful as uterus relaxants, vasoconstrictors, parkinsonism inhibitors (no data), and bronchodilators, were prepd. Condensing 5,6-dimethoxy-3,4-dihydro-2(1H)-naphthalenone with 4-HOC6H4CH2CH(NH2)Me.HBr in MeOH contg. K2CO3 and reducing the product in situ with NaBH3CN gave II (R4 = Me), isolated as the HCl salt. This diether was cleaved with HBr to give 82% II (R4 = H).HBr which had ID50 of 1.6 nmol/kg (guinea pigs) against histamine-induced bronchospasm.

L2 ANSWER 26 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 90060-17-6 REGISTRY
CN Propanoic acid, 2-methyl-, 5,6,7,8-tetrahydro-6-[[2-(4-methoxyphenyl)-1-methylethyl]amino]-1,2-naphthalenediyl ester, hydrochloride (9CI) (CA INDEX NAME)
MF C28 H37 N O5 . Cl H
LC STN Files: CA, CAPLUS
CRN (90060-36-9)



● HCl

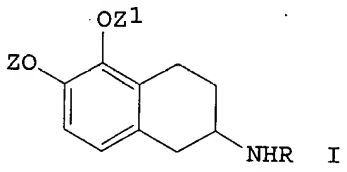
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1

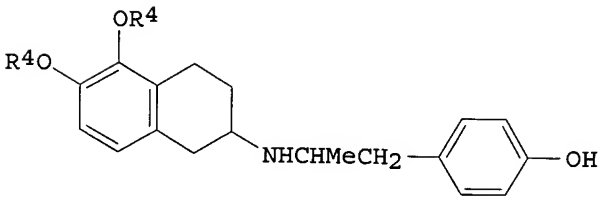
AN 100:191603 CA
TI 1,2,3,4-Tetrahydronaphthalene derivatives and compositions containing them
IN Chiesi, Paolo; Villani, Vlavio
PA Chiesi Farmaceutici S.p.A., Italy
SO Ger. Offen., 33 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3320936	A1	19831222	DE 1983-3320936	19830609
	DE 3320936	C2	19921119		
	GB 2123410	A1	19840201	GB 1983-15673	19830608
	GB 2123410	B2	19860828		
	FR 2528422	A1	19831216	FR 1983-9626	19830610
	FR 2528422	B1	19871030		
PRAI	IT 1982-21801		19820610		

GI



I

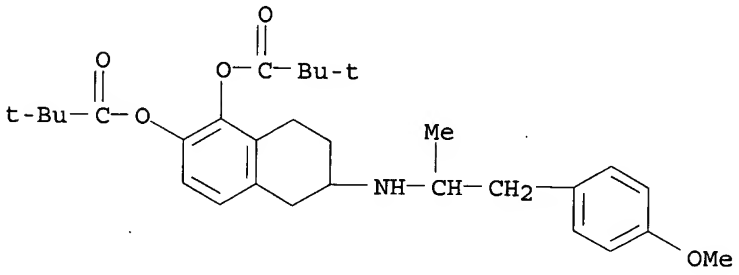


II

AB Tetrahydronaphthalenes I [R = H, C1-4 alkyl, C4-7 cycloalkyl, CR1R2(CH2)nPh; R1, R2 = H, C1-4 alkyl; n = 1, 2; the Ph (un)substituted by 1 or several halo, OH, MeO, OCH2O; Z, Z1 = H, C1-4 alkyl, C3-7 cycloalkyl, Z2R3; Z2 = CO, SO2; R3 = C1-15 alkyl, Ph (un)substituted by C1-4 alkyl] and their physiol. tolerable salts, having sympathomimetic activity and useful as uterus relaxants, vasoconstrictors, parkinsonism inhibitors (no data), and bronchodilators, were prepd. Condensing 5,6-dimethoxy-3,4-dihydro-2(1H)-naphthalenone with 4-HOC6H4CH2CH(NH2)Me.HBr in MeOH contg.

K2CO3 and reducing the product in situ with NaBH3CN gave II (R4 = Me), isolated as the HCl salt. This diether was cleaved with HBr to give 82% II (R4 = H).HBr which had ID50 of 1.6 nmol/kg (guinea pigs) against histamine-induced bronchospasm.

L2 ANSWER 27 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 90060-16-5 REGISTRY
CN Propanoic acid, 2,2-dimethyl-, 5,6,7,8-tetrahydro-6-[[2-(4-methoxyphenyl)-1-methylethyl]amino]-1,2-naphthalenediyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C30 H41 N O5
CI COM
LC STN Files: CA, CAPLUS, CASREACT



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

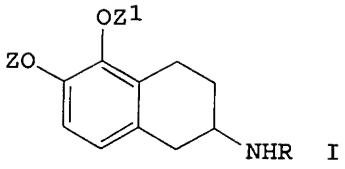
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1

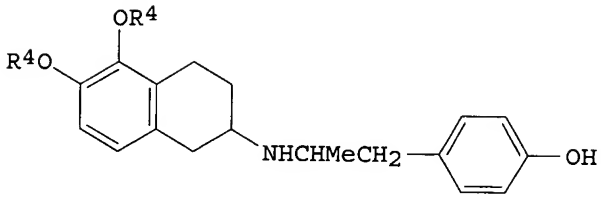
AN 100:191603 CA
TI 1,2,3,4-Tetrahydronaphthalene derivatives and compositions containing them
IN Chiesi, Paolo; Villani, Vlavio
PA Chiesi Farmaceutici S.p.A., Italy
SO Ger. Offen., 33 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3320936	A1	19831222	DE 1983-3320936	19830609
	DE 3320936	C2	19921119		
	GB 2123410	A1	19840201	GB 1983-15673	19830608
	GB 2123410	B2	19860828		
	FR 2528422	A1	19831216	FR 1983-9626	19830610
	FR 2528422	B1	19871030		
PRAI	IT 1982-21801		19820610		

GI



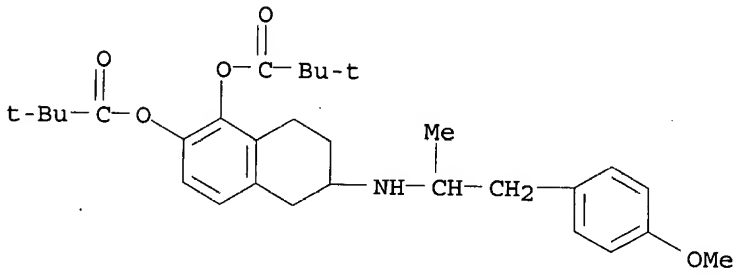
I



II

AB Tetrahydronaphthalenes I [R = H, C1-4 alkyl, C4-7 cycloalkyl, CR1R2(CH2)nPh; R1, R2 = H, C1-4 alkyl; n = 1, 2; the Ph (un)substituted by 1 or several halo, OH, MeO, OCH2O; Z, Z1 = H, C1-4 alkyl, C3-7 cycloalkyl, Z2R3; Z2 = CO, SO2; R3 = C1-15 alkyl, Ph (un)substituted by C1-4 alkyl] and their physiol. tolerable salts, having sympathomimetic activity and useful as uterus relaxants, vasoconstrictors, parkinsonism inhibitors (no data), and bronchodilators, were prepd. Condensing 5,6-dimethoxy-3,4-dihydro-2(1H)-naphthalenone with 4-HOC6H4CH2CH(NH2)Me.HBr in MeOH contg. K2CO3 and reducing the product in situ with NaBH3CN gave II (R4 = Me), isolated as the HCl salt. This diether was cleaved with HBr to give 82% II (R4 = H).HBr which had ID50 of 1.6 nmol/kg (guinea pigs) against histamine-induced bronchospasm.

L2 ANSWER 28 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 90060-15-4 REGISTRY
CN Propanoic acid, 2,2-dimethyl-, 5,6,7,8-tetrahydro-6-[[2-(4-methoxyphenyl)-1-methylethyl]amino]-1,2-naphthalenediyl ester, hydrochloride (9CI) (CA INDEX NAME)
MF C30 H41 N O5 . Cl H
LC STN Files: CA, CAPLUS
CRN (90060-16-5)



● HCl

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

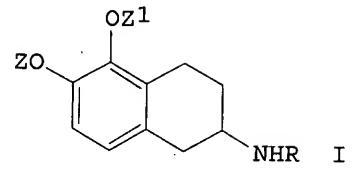
REFERENCE 1

AN 100:191603 CA
TI 1,2,3,4-Tetrahydronaphthalene derivatives and compositions containing them
IN Chiesi, Paolo; Villani, Vlavio
PA Chiesi Farmaceutici S.p.A., Italy
SO Ger. Offen., 33 pp.
CODEN: GWXXBX
DT Patent
LA German

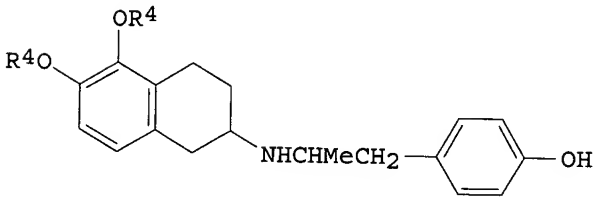
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3320936	A1	19831222	DE 1983-3320936	19830609
	DE 3320936	C2	19921119		
	GB 2123410	A1	19840201	GB 1983-15673	19830608
	GB 2123410	B2	19860828		
	FR 2528422	A1	19831216	FR 1983-9626	19830610
	FR 2528422	B1	19871030		
PRAI	IT 1982-21801	19820610			

GI



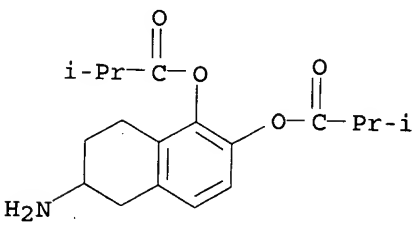
I



II

AB Tetrahydronaphthalenes I [R = H, C1-4 alkyl, C4-7 cycloalkyl, CR1R2(CH2)nPh; R1, R2 = H, C1-4 alkyl; n = 1, 2; the Ph (un)substituted by 1 or several halo, OH, MeO, OCH2O; Z, Z1 = H, C1-4 alkyl, C3-7 cycloalkyl, Z2R3; Z2 = CO, SO2; R3 = C1-15 alkyl, Ph (un)substituted by C1-4 alkyl] and their physiol. tolerable salts, having sympathomimetic activity and useful as uterus relaxants, vasoconstrictors, parkinsonism inhibitors (no data), and bronchodilators, were prepd. Condensing 5,6-dimethoxy-3,4-dihydro-2(1H)-naphthalenone with 4-HOC6H4CH2CH(NH2)Me.HBr in MeOH contg. K2CO3 and reducing the product in situ with NaBH3CN gave II (R4 = Me), isolated as the HCl salt. This diether was cleaved with HBr to give 82% II (R4 = H).HBr which had ID50 of 1.6 nmol/kg (guinea pigs) against histamine-induced bronchospasm.

L2 ANSWER 29 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 90060-14-3 REGISTRY
CN Propanoic acid, 2-methyl-, 6-amino-5,6,7,8-tetrahydro-1,2-naphthalenediyl ester, hydrobromide (9CI) (CA INDEX NAME)
MF C18 H25 N O4 . Br H
LC STN Files: CA, CAPLUS, CASREACT
CRN (90060-34-7)



HBr

1 REFERENCES IN FILE CA (1957 TO DATE)

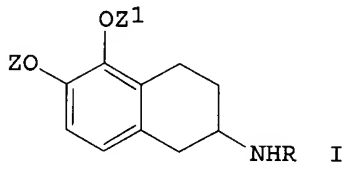
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1

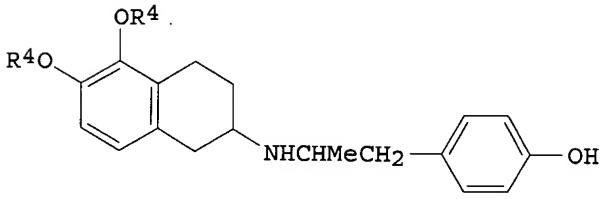
AN 100:191603 CA
TI 1,2,3,4-Tetrahydronaphthalene derivatives and compositions containing them
IN Chiesi, Paolo; Villani, Vlavio
PA Chiesi Farmaceutici S.p.A., Italy
SO Ger. Offen., 33 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3320936	A1	19831222	DE 1983-3320936	19830609
	DE 3320936	C2	19921119		
	GB 2123410	A1	19840201	GB 1983-15673	19830608
	GB 2123410	B2	19860828		
	FR 2528422	A1	19831216	FR 1983-9626	19830610
	FR 2528422	B1	19871030		
PRAI	IT 1982-21801		19820610		

GI



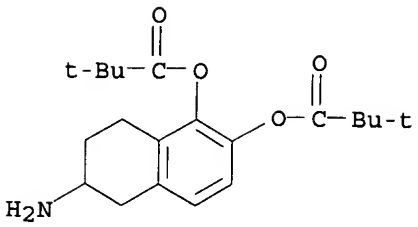
I



II

AB Tetrahydronaphthalenes I [R = H, C1-4 alkyl, C4-7 cycloalkyl, CR1R2(CH2)nPh; R1, R2 = H, C1-4 alkyl; n = 1, 2; the Ph (un)substituted by 1 or several halo, OH, MeO, OCH2O; Z, Z1 = H, C1-4 alkyl, C3-7 cycloalkyl, Z2R3; Z2 = CO, SO2; R3 = C1-15 alkyl, Ph (un)substituted by C1-4 alkyl] and their physiol. tolerable salts, having sympathomimetic activity and useful as uterus relaxants, vasoconstrictors, parkinsonism inhibitors (no data), and bronchodilators, were prepd. Condensing 5,6-dimethoxy-3,4-dihydro-2(1H)-naphthalenone with 4-HOC6H4CH2CH(NH2)Me.HBr in MeOH contg. K2CO3 and reducing the product in situ with NaBH3CN gave II (R4 = Me), isolated as the HCl salt. This diether was cleaved with HBr to give 82% II (R4 = H).HBr which had ID50 of 1.6 nmol/kg (guinea pigs) against histamine-induced bronchospasm.

L2 ANSWER 30 OF 30 REGISTRY COPYRIGHT 2003 ACS
RN 90060-13-2 REGISTRY
CN Propanoic acid, 2,2-dimethyl-, 6-amino-5,6,7,8-tetrahydro-1,2-naphthalenediyl ester, hydrobromide (9CI) (CA INDEX NAME)
MF C20 H29 N O4 . Br H
LC STN Files: CA, CAPLUS, CASREACT
CRN (90060-33-6)



● HBr

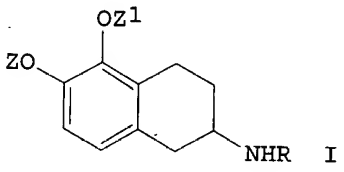
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1

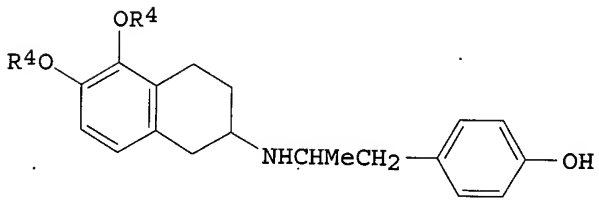
AN 100:191603 CA
TI 1,2,3,4-Tetrahydronaphthalene derivatives and compositions containing them
IN Chiesi, Paolo; Villani, Vlavio
PA Chiesi Farmaceutici S.p.A., Italy
SO Ger. Offen., 33 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3320936	A1	19831222	DE 1983-3320936	19830609
	DE 3320936	C2	19921119		
	GB 2123410	A1	19840201	GB 1983-15673	19830608
	GB 2123410	B2	19860828		
	FR 2528422	A1	19831216	FR 1983-9626	19830610
	FR 2528422	B1	19871030		
PRAI	IT 1982-21801		19820610		

GI



I



II

AB Tetrahydronaphthalenes I [R = H, C1-4 alkyl, C4-7 cycloalkyl, CR1R2(CH2)nPh; R1, R2 = H, C1-4 alkyl; n = 1, 2; the Ph (un)substituted by 1 or several halo, OH, MeO, OCH2O; Z, Z1 = H, C1-4 alkyl, C3-7 cycloalkyl, Z2R3; Z2 = CO, SO2; R3 = C1-15 alkyl, Ph (un)substituted by C1-4 alkyl] and their physiol. tolerable salts, having sympathomimetic activity and useful as uterus relaxants, vasoconstrictors, parkinsonism inhibitors (no data), and bronchodilators, were prepd. Condensing 5,6-dimethoxy-3,4-dihydro-2(1H)-naphthalenone with 4-HOC6H4CH2CH(NH2)Me.HBr in MeOH contg. K2CO3 and reducing the product in situ with NaBH3CN gave II (R4 = Me), isolated as the HCl salt. This diether was cleaved with HBr to give 82%

II (R4 = H).HBr which had ID50 of 1.6 nmol/kg (guinea pigs) against histamine-induced bronchospasm.

=>